



## Clinical trial results:

### A randomized phase 2 non-comparative study of the efficacy of PF-04691502 and PF-05212384 in patients with recurrent endometrial cancer

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2011-003062-32   |
| Trial protocol           | SK ES PL DE GB   |
| Global end of trial date | 25 December 2015 |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 14 December 2016 |
| First version publication date | 14 December 2016 |

#### Trial information

##### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | B1271004 |
|-----------------------|----------|

##### Additional study identifiers

|                                    |   |
|------------------------------------|---|
| ISRCTN number                      | - |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN)   | - |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Pfizer, Inc.  |
| Sponsor organisation address | 235 East 42nd Street, New York, United States, 10017  |
| Public contact               | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact           | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com |

Notes:

#### Paediatric regulatory details

|  |    |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 27 July 2016     |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 30 April 2014    |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 25 December 2015 |
| Was the trial ended prematurely?                     | Yes              |

Notes:

## General information about the trial

Main objective of the trial:

Arm A: To assess the clinical benefit response (CBR) of the oral PI3K/mTOR inhibitor PF-04691502 in patients with recurrent endometrial cancer that is classified as PI3K basal.

Arm B: To assess the CBR of the IV PI3K/mTOR inhibitor PF-05212384 in patients with recurrent endometrial cancer that is classified as PI3K basal.

Arm C: To assess the CBR of the oral PI3K/mTOR inhibitor PF-04691502 in patients with recurrent endometrial cancer that is classified as PI3K activated.

Arm D: To assess the CBR of the IV PI3K/mTOR inhibitor PF-05212384 in patients with recurrent endometrial cancer that is classified as PI3K activated.

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the declaration of Helsinki and in compliance with all International Council on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed; in particular, those affording greater protection to the safety of study participants.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 02 February 2012 |
| Long term follow-up planned                               | Yes              |
| Long term follow-up rationale                             | Efficacy         |
| Long term follow-up duration                              | 3 Years          |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Australia: 2      |
| Country: Number of subjects enrolled | Canada: 15        |
| Country: Number of subjects enrolled | Japan: 12         |
| Country: Number of subjects enrolled | Poland: 2         |
| Country: Number of subjects enrolled | Spain: 22         |
| Country: Number of subjects enrolled | United States: 14 |
| Worldwide total number of subjects   | 67                |
| EEA total number of subjects         | 24                |

Notes:

| <b>Subjects enrolled per age group</b>    |    |
|---|----|
| In utero                                  | 0  |
| Preterm newborn - gestational age < 37 wk | 0  |
| Newborns (0-27 days)                      | 0  |
| Infants and toddlers (28 days-23 months)  | 0  |
| Children (2-11 years)                     | 0  |
| Adolescents (12-17 years)                 | 0  |
| Adults (18-64 years)                      | 29 |
| From 65 to 84 years                       | 37 |
| 85 years and over                         | 1  |

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted at 6 centers in Australia, Canada, Japan, Poland, Spain and the United States. All enrolled participants from 6 centers were included in the trial.

### Pre-assignment

Screening details:

This study was conducted in parallel-arms in adult participants with recurrent endometrial cancer. Randomized arms included PF-05212384 (154mg dosage) and PF-04691502 (8mg which was lowered to 6mg) for both PI3K Basal or Activated. Lead-in Cohorts included PF-05212384 (89mg or 154mg) and PF-04691502 (4mg).

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Randomised - controlled        |
| Blinding used                | Not blinded                    |

### Arms

|                              |                               |
|------------------------------|-------------------------------|
| Are arms mutually exclusive? | Yes                           |
| <b>Arm title</b>             | PF-04691502 8 mg (PI3K Basal) |

Arm description:

Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K basal). Participants self-administered PF-04691502 8 mg orally, once daily (QD) until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death. Dose of the participants were reduced to 6 mg if they were on 8 mg dose.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | PF-04691502  |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Participants self-administered PF-04691502 8 mg orally, once daily (QD) until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.

|  |             |
|--|-------------|
| Investigational medicinal product name | PF-04691502 |
| Investigational medicinal product code |             |
| Other name                             |             |
| Pharmaceutical forms                   | Tablet      |
| Routes of administration               | Oral use    |

Dosage and administration details:

Participants received PF-04691502 8 mg by 30 minute infusion at the study site, once weekly (Quaque, QW) until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.

|                  |                               |
|------------------|-------------------------------|
| <b>Arm title</b> | PF-04691502 6 mg (PI3K Basal) |
|------------------|-------------------------------|

Arm description:

Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K basal). Participants self-administered PF-04691502 6 mg orally, QD until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|   |                                     |
|---|-------------------------------------|
| Investigational medicinal product name  | PF-04691502                         |
| Investigational medicinal product code  |                                     |
| Other name  |                                     |
| Pharmaceutical forms  | Tablet                              |
| Routes of administration  | Oral use                            |
| Dosage and administration details:  |                                     |
| Participants self-administered PF-04691502 6 mg orally, QD until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.  |                                     |
| <b>Arm title</b>  | PF-04691502 8 mg (PI3K Activated)   |
| Arm description:  |                                     |
| Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K activated). Participants self-administered PF-04691502 8 mg orally, QD until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death. Dose of the participants were reduced to 6 mg if they were on 8 mg dose. |                                     |
| Arm type  | Experimental                        |
| Investigational medicinal product name  | PF-04691502                         |
| Investigational medicinal product code  |                                     |
| Other name  |                                     |
| Pharmaceutical forms  | Tablet                              |
| Routes of administration  | Oral use                            |
| Dosage and administration details:  |                                     |
| Participants self-administered PF-04691502 8 mg orally, QD until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death. Dose of the participants were reduced to 6 mg if they were on 8 mg dose.   |                                     |
| <b>Arm title</b>  | PF-04691502 6 mg (PI3K Activated)   |
| Arm description:  |                                     |
| Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K activated). Participants self-administered PF-04691502 6 mg orally, QD until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.  |                                     |
| Arm type  | Experimental                        |
| Investigational medicinal product name  | PF-04691502                         |
| Investigational medicinal product code  |                                     |
| Other name  |                                     |
| Pharmaceutical forms  | Tablet                              |
| Routes of administration  | Oral use                            |
| Dosage and administration details:  |                                     |
| Participants self-administered PF-04691502 6 mg orally, QD until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.  |                                     |
| <b>Arm title</b>  | PF-05212384 154 mg (PI3K Basal)     |
| Arm description:  |                                     |
| Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K basal). Participants received PF-05212384 154 mg by 30 minute infusion at the study site, once weekly (Quaque, QW) until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.                              |                                     |
| Arm type  | Experimental                        |
| Investigational medicinal product name  | PF-05212384                         |
| Investigational medicinal product code  |                                     |
| Other name  |                                     |
| Pharmaceutical forms  | Infusion                            |
| Routes of administration  | Intravenous use                     |
| Dosage and administration details:  |                                     |
| Participants received PF-05212384 154 mg by 30 minute infusion at the study site, once weekly (Quaque, QW) until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.  |                                     |
| <b>Arm title</b>  | PF-05212384 154 mg (PI3K Activated) |

**Arm description:**

Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K activated). Participants received PF-05212384 154 mg by 30 minute infusion at the study site, QW until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.

|  |                 |
|--|-----------------|
| Arm type                               | Experimental    |
| Investigational medicinal product name | PF-05212384     |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Infusion        |
| Routes of administration               | Intravenous use |

**Dosage and administration details:**

Participants received PF-05212384 154 mg by 30 minute infusion at the study site, QW until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.

|                  |   |
|------------------|---|
| <b>Arm title</b> | Lead-in-cohort (LIC) PF-04691502 (4 mg) |
|------------------|---|

**Arm description:**

Participants who were enrolled in the PF-04691502 LIC began dosing with PF-04691502 4 mg at least 4 days (but no more than 10 days) prior to Cycle 1 Day 1 and continued taking PF-05691502 until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | PF-04691502  |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

**Dosage and administration details:**

Participants who were enrolled in the PF-04691502 LIC began dosing with PF-04691502 4 mg at least 4 days (but no more than 10 days) prior to Cycle 1 Day 1 and continued taking PF-05691502 until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.

|                  |                         |
|------------------|-------------------------|
| <b>Arm title</b> | LIC PF-05212384 (89 mg) |
|------------------|-------------------------|

**Arm description:**

Participants who were enrolled in the PF-05212384 LIC began dosing with PF-05212384 89 mg at least 4 days (but no more than 10 days) prior to Cycle 1 Day 1 and continued taking PF-05212384 until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | PF-05212384  |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Infusion     |
| Routes of administration               | Oral use     |

**Dosage and administration details:**

Participants who were enrolled in the PF-05212384 LIC began dosing with PF-05212384 89 mg at least 4 days (but no more than 10 days) prior to Cycle 1 Day 1 and continued taking PF-05212384 until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.

|                  |                          |
|------------------|--------------------------|
| <b>Arm title</b> | LIC PF-05212384 (154 mg) |
|------------------|--------------------------|

**Arm description:**

Participants who were enrolled in the PF-05212384 LIC began dosing with PF-05212384 154 mg at least 4 days (but no more than 10 days) prior to Cycle 1 Day 1 and continued taking PF-05212384 until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|  |          |
|--|----------|
| Investigational medicinal product name | 05212384 |
| Investigational medicinal product code |          |
| Other name                             |          |
| Pharmaceutical forms                   | Infusion |
| Routes of administration               | Oral use |

Dosage and administration details:

Participants who were enrolled in the PF-05212384 LIC began dosing with PF-05212384 154 mg at least 4 days (but no more than 10 days) prior to Cycle 1 Day 1 and continued taking PF-05212384 until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.

| <b>Number of subjects in period 1</b> | PF-04691502 8 mg<br>(PI3K Basal) | PF-04691502 6 mg<br>(PI3K Basal) | PF-04691502 8 mg<br>(PI3K Activated) |
|---------------------------------------|----------------------------------|----------------------------------|--------------------------------------|
| Started                               | 3                                | 1                                | 11                                   |
| Completed                             | 0                                | 0                                | 0                                    |
| Not completed                         | 3                                | 1                                | 11                                   |
| Other Reasons                         | -                                | -                                | 1                                    |
| Death                                 | 1                                | -                                | 8                                    |
| Study Terminated by Sponsor           | 2                                | 1                                | 1                                    |
| Lost to follow-up                     | -                                | -                                | -                                    |
| Subject Refused Further Follow-up     | -                                | -                                | 1                                    |

| <b>Number of subjects in period 1</b> | PF-04691502 6 mg<br>(PI3K Activated) | PF-05212384 154<br>mg (PI3K Basal) | PF-05212384 154<br>mg (PI3K Activated) |
|---------------------------------------|--------------------------------------|------------------------------------|--|
| Started                               | 3                                    | 20                                 | 20                                     |
| Completed                             | 0                                    | 0                                  | 0                                      |
| Not completed                         | 3                                    | 20                                 | 20                                     |
| Other Reasons                         | -                                    | -                                  | -                                      |
| Death                                 | -                                    | 7                                  | 12                                     |
| Study Terminated by Sponsor           | 3                                    | 11                                 | 7                                      |
| Lost to follow-up                     | -                                    | 1                                  | 1                                      |
| Subject Refused Further Follow-up     | -                                    | 1                                  | -                                      |

| <b>Number of subjects in period 1</b> | Lead-in-cohort (LIC)<br>PF-04691502 (4 mg) | LIC PF-05212384<br>(89 mg) | LIC PF-05212384<br>(154 mg) |
|---------------------------------------|--|----------------------------|-----------------------------|
| Started                               | 3  | 3                          | 3                           |
| Completed                             | 0  | 0                          | 0                           |
| Not completed                         | 3  | 3                          | 3                           |
| Other Reasons                         | -  | -                          | -                           |
| Death                                 | -  | 1                          | 1                           |
| Study Terminated by Sponsor           | 3  | 2                          | 2                           |
| Lost to follow-up                     | -  | -                          | -                           |
| Subject Refused Further Follow-up     | -  | -                          | -                           |





## Baseline characteristics

### Reporting groups

|  |   |
|--|---|
| Reporting group title  | PF-04691502 8 mg (PI3K Basal)           |
| Reporting group description:<br>Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K basal). Participants self-administered PF-04691502 8 mg orally, once daily (QD) until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death. Dose of the participants were reduced to 6 mg if they were on 8 mg dose. |   |
| Reporting group title  | PF-04691502 6 mg (PI3K Basal)           |
| Reporting group description:<br>Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K basal). Participants self-administered PF-04691502 6 mg orally, QD until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.   |   |
| Reporting group title  | PF-04691502 8 mg (PI3K Activated)       |
| Reporting group description:<br>Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K activated). Participants self-administered PF-04691502 8 mg orally, QD until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death. Dose of the participants were reduced to 6 mg if they were on 8 mg dose.          |   |
| Reporting group title  | PF-04691502 6 mg (PI3K Activated)       |
| Reporting group description:<br>Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K activated). Participants self-administered PF-04691502 6 mg orally, QD until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.   |   |
| Reporting group title  | PF-05212384 154 mg (PI3K Basal)         |
| Reporting group description:<br>Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K basal). Participants received PF-05212384 154 mg by 30 minute infusion at the study site, once weekly (Quaque, QW) until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.                                       |   |
| Reporting group title  | PF-05212384 154 mg (PI3K Activated)     |
| Reporting group description:<br>Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K activated). Participants received PF-05212384 154 mg by 30 minute infusion at the study site, QW until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.   |   |
| Reporting group title  | Lead-in-cohort (LIC) PF-04691502 (4 mg) |
| Reporting group description:<br>Participants who were enrolled in the PF-04691502 LIC began dosing with PF-04691502 4 mg at least 4 days (but no more than 10 days) prior to Cycle 1 Day 1 and continued taking PF-05691502 until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.  |   |
| Reporting group title  | LIC PF-05212384 (89 mg)                 |
| Reporting group description:<br>Participants who were enrolled in the PF-05212384 LIC began dosing with PF-05212384 89 mg at least 4 days (but no more than 10 days) prior to Cycle 1 Day 1 and continued taking PF-05212384 until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.   |   |
| Reporting group title  | LIC PF-05212384 (154 mg)                |
| Reporting group description:<br>Participants who were enrolled in the PF-05212384 LIC began dosing with PF-05212384 154 mg at least 4 days (but no more than 10 days) prior to Cycle 1 Day 1 and continued taking PF-05212384 until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.  |   |

| Reporting group values                 | PF-04691502 8 mg<br>(PI3K Basal) | PF-04691502 6 mg<br>(PI3K Basal) | PF-04691502 8 mg<br>(PI3K Activated) |
|--|----------------------------------|----------------------------------|--------------------------------------|
| Number of subjects                     | 3                                | 1                                | 11                                   |
| Age Categorical<br>Units: Subjects     |                                  |                                  |                                      |
| < 18 years                             | 0                                | 0                                | 0                                    |
| 18 - 44 years                          | 0                                | 0                                | 0                                    |
| 45 - 64 years                          | 2                                | 1                                | 4                                    |
| >= 65 years                            | 1                                | 0                                | 7                                    |
| Age continuous<br>Units: years         |                                  |                                  |                                      |
| arithmetic mean                        | 3                                | 1                                | 11                                   |
| standard deviation                     | ± 61.7                           | ± 54                             | ± 66.5                               |
| Gender, Male/Female<br>Units: Subjects |                                  |                                  |                                      |
| Female                                 | 3                                | 1                                | 11                                   |
| Male                                   | 0                                | 0                                | 0                                    |

| Reporting group values                 | PF-04691502 6 mg<br>(PI3K Activated) | PF-05212384 154<br>mg (PI3K Basal) | PF-05212384 154<br>mg (PI3K Activated) |
|--|--------------------------------------|------------------------------------|--|
| Number of subjects                     | 3                                    | 20                                 | 20                                     |
| Age Categorical<br>Units: Subjects     |                                      |                                    |  |
| < 18 years                             | 0                                    | 0                                  | 0                                      |
| 18 - 44 years                          | 0                                    | 0                                  | 0                                      |
| 45 - 64 years                          | 3                                    | 9                                  | 4                                      |
| >= 65 years                            | 0                                    | 11                                 | 16                                     |
| Age continuous<br>Units: years         |                                      |                                    |  |
| arithmetic mean                        | 3                                    | 20                                 | 20                                     |
| standard deviation                     | ± 60                                 | ± 65.7                             | ± 69.6                                 |
| Gender, Male/Female<br>Units: Subjects |                                      |                                    |  |
| Female                                 | 3                                    | 20                                 | 20                                     |
| Male                                   | 0                                    | 0                                  | 0                                      |

| Reporting group values                 | Lead-in-cohort (LIC)<br>PF-04691502 (4 mg) | LIC PF-05212384<br>(89 mg) | LIC PF-05212384<br>(154 mg) |
|--|--|----------------------------|-----------------------------|
| Number of subjects                     | 3  | 3                          | 3                           |
| Age Categorical<br>Units: Subjects     |  |                            |                             |
| < 18 years                             | 0  | 0                          | 0                           |
| 18 - 44 years                          | 0  | 1                          | 0                           |
| 45 - 64 years                          | 2  | 1                          | 2                           |
| >= 65 years                            | 1  | 1                          | 1                           |
| Age continuous<br>Units: years         |  |                            |                             |
| arithmetic mean                        | 3  | 3                          | 3                           |
| standard deviation                     | ± 64.3                                     | ± 56.7                     | ± 62.7                      |
| Gender, Male/Female<br>Units: Subjects |  |                            |                             |
| Female                                 | 3  | 3                          | 3                           |

|      |   |   |   |
|------|---|---|---|
| Male | 0 | 0 | 0 |
|------|---|---|---|

|   |       |  |  |
|---|-------|--|--|
| <b>Reporting group values</b>   | Total |  |  |
| Number of subjects  | 67    |  |  |
| Age Categorical<br>Units: Subjects                                      |       |  |  |
| < 18 years  | 0     |  |  |
| 18 - 44 years   | 1     |  |  |
| 45 - 64 years   | 28    |  |  |
| >= 65 years   | 38    |  |  |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | -     |  |  |
| Gender, Male/Female<br>Units: Subjects                                  |       |  |  |
| Female  | 67    |  |  |
| Male  | 0     |  |  |

## End points

### End points reporting groups

|  |   |
|--|---|
| Reporting group title  | PF-04691502 8 mg (PI3K Basal)           |
| Reporting group description:<br>Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K basal). Participants self-administered PF-04691502 8 mg orally, once daily (QD) until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death. Dose of the participants were reduced to 6 mg if they were on 8 mg dose. |   |
| Reporting group title  | PF-04691502 6 mg (PI3K Basal)           |
| Reporting group description:<br>Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K basal). Participants self-administered PF-04691502 6 mg orally, QD until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.   |   |
| Reporting group title  | PF-04691502 8 mg (PI3K Activated)       |
| Reporting group description:<br>Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K activated). Participants self-administered PF-04691502 8 mg orally, QD until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death. Dose of the participants were reduced to 6 mg if they were on 8 mg dose.          |   |
| Reporting group title  | PF-04691502 6 mg (PI3K Activated)       |
| Reporting group description:<br>Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K activated). Participants self-administered PF-04691502 6 mg orally, QD until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.   |   |
| Reporting group title  | PF-05212384 154 mg (PI3K Basal)         |
| Reporting group description:<br>Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K basal). Participants received PF-05212384 154 mg by 30 minute infusion at the study site, once weekly (Quaque, QW) until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.                                       |   |
| Reporting group title  | PF-05212384 154 mg (PI3K Activated)     |
| Reporting group description:<br>Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K activated). Participants received PF-05212384 154 mg by 30 minute infusion at the study site, QW until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.   |   |
| Reporting group title  | Lead-in-cohort (LIC) PF-04691502 (4 mg) |
| Reporting group description:<br>Participants who were enrolled in the PF-04691502 LIC began dosing with PF-04691502 4 mg at least 4 days (but no more than 10 days) prior to Cycle 1 Day 1 and continued taking PF-05691502 until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.  |   |
| Reporting group title  | LIC PF-05212384 (89 mg)                 |
| Reporting group description:<br>Participants who were enrolled in the PF-05212384 LIC began dosing with PF-05212384 89 mg at least 4 days (but no more than 10 days) prior to Cycle 1 Day 1 and continued taking PF-05212384 until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.   |   |
| Reporting group title  | LIC PF-05212384 (154 mg)                |
| Reporting group description:<br>Participants who were enrolled in the PF-05212384 LIC began dosing with PF-05212384 154 mg at least 4 days (but no more than 10 days) prior to Cycle 1 Day 1 and continued taking PF-05212384 until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.  |   |
| Subject analysis set title   | Safety analysis set                     |
| Subject analysis set type  | Safety analysis                         |

Subject analysis set description:

Participants were analyzed on safety analysis set which was defined as all enrolled patients who started treatment.

|                            |                  |
|----------------------------|------------------|
| Subject analysis set title | Per Protocol Set |
| Subject analysis set type  | Per protocol     |

Subject analysis set description:

Per protocol dataset included participants enrolled for treatment, with baseline tumor, measurable disease and with disease under study. The LIC eporting arm were not a part of the per protocol analysis set for summarizing response.

|                            |                               |
|----------------------------|-------------------------------|
| Subject analysis set title | Pharmacokinetics Analysis Set |
| Subject analysis set type  | Sub-group analysis            |

Subject analysis set description:

Subjects were analyzed on PK parameter analysis set which was defined as all treated patients who had at least one of the PK parameters of interest estimated.

|                            |   |
|----------------------------|---|
| Subject analysis set title | Pharmacodynamic Analysis Biomarkers Set |
| Subject analysis set type  | Sub-group analysis                      |

Subject analysis set description:

Subjects were analyzed on PD analysis set which consisted of all enrolled patients who started treatment and had a baseline as well as at least one post-baseline measurement for at least one PD biomarker. The PD biomarkers include serum glucose, insulin, HbA1c, cholesterol, and triglycerides.

|                            |  |
|----------------------------|--|
| Subject analysis set title | Molecular Profiling Tumor Analysis Set |
| Subject analysis set type  | Sub-group analysis                     |

Subject analysis set description:

Subjects were analyzed as the molecular profiling tumor analysis set was defined as all enrolled patients who started treatment and had baseline tumor tissues (archived paraffin block or unstained slides or fresh tumor tissue sample) successfully analyzed for at least one of the biomarkers.

|                            |                                      |
|----------------------------|--------------------------------------|
| Subject analysis set title | PF-05212384 (PI3K Basal + Activated) |
| Subject analysis set type  | Per protocol                         |

Subject analysis set description:

Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K basal + activated). Participants were given PF-05212384 QW (Days 1, 8, 15 and 22 of each cycle), with a  $\pm 3$  day window.

|                            |                          |
|----------------------------|--------------------------|
| Subject analysis set title | PF-04691502 (PI3K Basal) |
| Subject analysis set type  | Sub-group analysis       |

Subject analysis set description:

Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K basal). Participants self-administered PF-04691502 orally, once daily (QD) until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.

|                            |                              |
|----------------------------|------------------------------|
| Subject analysis set title | PF-04691502 (PI3K Activated) |
| Subject analysis set type  | Sub-group analysis           |

Subject analysis set description:

Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K activated). Participants self-administered PF-04691502 8 mg orally, QD until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.

### Primary: Clinical Benefit Response for PF-04691502

|                 |  |
|-----------------|--|
| End point title | Clinical Benefit Response for PF-04691502 <sup>[1]</sup> |
|-----------------|--|

End point description:

Clinical benefit response was defined as best overall response of complete response (CR), partial response (PR) or stable disease (SD) for at least 16 weeks from Cycle 1 Day 1 (C1D1) to the first time of disease progression. The outcome data table below presents the number of participants with clinical benefit response as "yes" or "no". On 09 Oct 2012, Pfizer decided to stop enrollment into PF-04691502. While tumor assessment for PF-04691502 was included as a listing in the final report, formal efficacy analysis for PF-04691502 was not performed.

Per protocol dataset included participants enrolled for treatment, with baseline tumor, measurable disease and with disease under study. The LIC reporting arm were not a part of the per protocol analysis set for summarizing response.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

16 weeks from Cycle 1 Day 1

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: This endpoint has no statistical analysis.

| End point values                 | PF-04691502<br>(PI3K Basal) | PF-04691502<br>(PI3K<br>Activated) |  |  |
|----------------------------------|-----------------------------|------------------------------------|--|--|
| Subject group type               | Subject analysis set        | Subject analysis set               |  |  |
| Number of subjects analysed      | 4                           | 11                                 |  |  |
| Units: Participants              |                             |                                    |  |  |
| Participants with "Yes" response | 1                           | 0                                  |  |  |
| Participants with "No" response  | 3                           | 11                                 |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of participants with clinical benefit response for PF-05212384

|                 |   |
|-----------------|---|
| End point title | Percentage of participants with clinical benefit response for PF-05212384 <sup>[2]</sup> <sup>[3]</sup> |
|-----------------|---|

End point description:

Clinical benefit response was defined as best overall response of complete response (CR), partial response (PR) or stable disease (SD) for at least 16 weeks from Cycle 1 Day 1 (C1D1) to the first time of disease progression. The primary analysis is based on the clinical benefit rate which is calculated as proportion of participants with a clinical benefit response relative to total number of response evaluable participants. Per RECIST v1.1 for target lesions: CR defined as disappearance of all target lesions; PR defined as  $\geq 30\%$  decrease in the sum of the longest diameter of target lesions; SD does not qualify for CR, PR or Progression. All target lesions must be assessed. SD can follow PR only in the rare case that the sum increases by less than 20% from the nadir, but enough that a previously documented 30% decrease no longer holds. A Clopper-Pearson exact 95% CI for the clinical benefit rate is presented in the below table.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

16 weeks from Cycle 1 Day 1

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: This endpoint has no statistical analysis.

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint has no statistical analysis.

| End point values                  | PF-05212384<br>154 mg (PI3K<br>Basal) | PF-05212384<br>154 mg (PI3K<br>Activated) | PF-05212384<br>(PI3K Basal +<br>Activated) |  |
|-----------------------------------|---------------------------------------|---|--|--|
| Subject group type                | Reporting group                       | Reporting group                           | Subject analysis set                       |  |
| Number of subjects analysed       | 10                                    | 5   | 15   |  |
| Units: Percentage of participants |                                       |   |  |  |
| number (confidence interval 95%)  | 52.6 (28.9 to<br>75.6)                | 26.3 (9.1 to<br>51.2)                     | 39.5 (24 to<br>56.6)                       |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Objective Response for PF-04691502

|                 |                                    |
|-----------------|------------------------------------|
| End point title | Objective Response for PF-04691502 |
|-----------------|------------------------------------|

End point description:

Objective response is defined as CR or PR. CR: Complete response: 2 or more objective statuses of CR a minimum of 4 weeks apart documented before PD. Partial response: 2 or more objective statuses of PR or better a minimum of 4 weeks apart documented before PD, but not qualifying as CR. Per RECIST v1.1 for target lesions: CR defined as disappearance of all target lesions; PR defined as  $\geq 30\%$  decrease in the sum of the longest diameter of target lesions. The outcome data table below presents the number of participants with objective response as "yes" or "no". On 09 Oct 2012, Pfizer decided to stop enrollment into PF-04691502. While tumor assessment for PF-04691502 was included as a listing in the final report, formal efficacy analysis for PF-04691502 was not performed.

The LIC reporting arm were not a part of the per protocol analysis set for summarizing response.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Randomization to objective progression, death or last tumor assessment without progression (up to 12 months)

| End point values                 | PF-04691502<br>(PI3K Basal) | PF-04691502<br>(PI3K<br>Activated) |  |  |
|----------------------------------|-----------------------------|------------------------------------|--|--|
| Subject group type               | Subject analysis set        | Subject analysis set               |  |  |
| Number of subjects analysed      | 4                           | 11                                 |  |  |
| Units: Participants response     |                             |                                    |  |  |
| Participants with "Yes" response | 0                           | 0                                  |  |  |
| Participants with "No" response  | 4                           | 11                                 |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of participants with objective response for PF-05212384

|                 |   |
|-----------------|---|
| End point title | Percentage of participants with objective response for PF-05212384 <sup>[4]</sup> |
|-----------------|---|

End point description:

Objective response is defined as CR or PR. CR: Complete response: 2 or more objective statuses of CR a minimum of 4 weeks apart documented before PD. Partial response: 2 or more objective statuses of PR or better a minimum of 4 weeks apart documented before PD, but not qualifying as CR. Per RECIST v1.1 for target lesions: CR defined as disappearance of all target lesions; PR defined as  $\geq 30\%$  decrease in the sum of the longest diameter of target lesions.

The LIC reporting arm were not a part of the per protocol analysis set for summarizing response.

|   |           |
|---|-----------|
| End point type  | Secondary |
| End point timeframe:  |           |
| Randomization to objective progression, death or last tumor assessment without progression (up to 12 months)  |           |
| Notes:  |           |
| [4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint has no statistical analysis. |           |

|                                   |                                    |  |   |  |
|-----------------------------------|------------------------------------|--|---|--|
| <b>End point values</b>           | PF-05212384<br>154 mg (PI3K Basal) | PF-05212384<br>154 mg (PI3K Activated) | PF-05212384<br>(PI3K Basal + Activated) |  |
| Subject group type                | Reporting group                    | Reporting group                        | Subject analysis set                    |  |
| Number of subjects analysed       | 19                                 | 19                                     | 38                                      |  |
| Units: Percentage of participants |                                    |  |   |  |
| number (confidence interval 95%)  | 21.1 (6.1 to 45.6)                 | 15.8 (3.4 to 39.6)                     | 18.4 (7.7 to 34.3)                      |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Progression free survival for PF-04691502

|  |   |
|--|---|
| End point title  | Progression free survival for PF-04691502 |
| End point description:   |   |
| PFS is defined as the time from the date of cycle 1 day 1 to the date that objective progressive disease is documented or death due to any cause, whichever occurs first. PFS was characterized in terms of the median. Approximate 95% confidence interval corresponding to this estimate was computed. Progression is defined using RECIST v1.1, as a 20% increase in the sum of the longest diameter of target lesions with a minimum absolute increase of 5 mm, or an unequivocal progression of non-target lesion, or the appearance of new lesions. On 09 Oct 2012, Pfizer decided to stop enrollment into PF-04691502. While tumor assessment for PF-04691502 was included as a listing in the final report, formal efficacy analysis for PF-04691502 was not performed. The LIC reporting arm were not a part of the per protocol analysis set for summarizing response. |   |
| End point type   | Secondary                                 |
| End point timeframe:   |   |
| From Cycle 1 Day 1 to objective progressive disease or death due to any cause whichever occurs first (up to 12 months)   |   |

|                             |                             |                                 |  |  |
|-----------------------------|-----------------------------|---------------------------------|--|--|
| <b>End point values</b>     | PF-04691502<br>(PI3K Basal) | PF-04691502<br>(PI3K Activated) |  |  |
| Subject group type          | Subject analysis set        | Subject analysis set            |  |  |
| Number of subjects analysed | 4                           | 11                              |  |  |
| Units: Time to Event (Days) |                             |                                 |  |  |
| Participant 1               | 1                           | 0                               |  |  |
| Participant 2               | 108                         | 0                               |  |  |
| Participant 3               | 50                          | 0                               |  |  |
| Participant 4               | 199                         | 0                               |  |  |
| Participant 5               | 0                           | 54                              |  |  |
| Participant 6               | 0                           | 55                              |  |  |



|                |   |     |  |  |
|----------------|---|-----|--|--|
| Participant 7  | 0 | 51  |  |  |
| Participant 8  | 0 | 1   |  |  |
| Participant 9  | 0 | 54  |  |  |
| Participant 10 | 0 | 62  |  |  |
| Participant 11 | 0 | 53  |  |  |
| Participant 12 | 0 | 105 |  |  |
| Participant 13 | 0 | 1   |  |  |
| Participant 14 | 0 | 54  |  |  |
| Participant 15 | 0 | 54  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Progression free survival for PF-05212384

|                 |  |
|-----------------|--|
| End point title | Progression free survival for PF-05212384 <sup>[5]</sup> |
|-----------------|--|

End point description:

PFS is defined as the time from the date of cycle 1 day 1 to the date that objective progressive disease is documented or death due to any cause, whichever occurs first. PFS was characterized in terms of the median. Approximate 95% confidence interval corresponding to this estimate was computed.

Progression is defined using RECIST v1.1, as a 20% increase in the sum of the longest diameter of target lesions with a minimum absolute increase of 5 mm, or an unequivocal progression of non-target lesion, or the appearance of new lesions.

The LIC reporting arm were not a part of the per protocol analysis set for summarizing response.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Cycle 1 Day 1 to objective progressive disease or death due to any cause whichever occurs first (up to 12 months)

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint has no statistical analysis.

| End point values                 | PF-05212384<br>154 mg (PI3K<br>Basal) | PF-05212384<br>154 mg (PI3K<br>Activated) | PF-05212384<br>(PI3K Basal +<br>Activated) |  |
|----------------------------------|---------------------------------------|---|--|--|
| Subject group type               | Reporting group                       | Reporting group                           | Subject analysis set                       |  |
| Number of subjects analysed      | 19                                    | 19  | 38   |  |
| Units: Days                      |                                       |   |  |  |
| median (confidence interval 95%) | 112 (59 to<br>167)                    | 89 (56 to 172)                            | 108 (62 to<br>149)                         |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of participants with progression free survival (PFS) at 6 months for PF-05212384

|                 |  |
|-----------------|--|
| End point title | Percentage of participants with progression free survival (PFS) at 6 months for PF-05212384 <sup>[6]</sup> |
|-----------------|--|

**End point description:**

Progression free survival is defined as the time from the date of cycle 1 day 1 to the date that objective progressive disease is documented or death due to any cause, whichever occurs first. PFS was characterized in terms of the probability of remaining progression-free at 6 months (based on Kaplan-Meier estimates). Progression is defined using RECIST v1.1, as a 20% increase in the sum of the longest diameter of target lesions with a minimum absolute increase of 5 mm, or an unequivocal progression of non-target lesion, or the appearance of new lesions.

Per protocol dataset included participants enrolled for treatment, with baseline tumor, measurable disease and with disease under study.

The LIC reporting arm were not a part of the per protocol analysis set for summarizing response.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

6 months

**Notes:**

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint has no statistical analysis.

| End point values                  | PF-05212384<br>154 mg (PI3K<br>Basal) | PF-05212384<br>154 mg (PI3K<br>Activated) | PF-05212384<br>(PI3K Basal +<br>Activated) |  |
|-----------------------------------|---------------------------------------|---|--|--|
| Subject group type                | Reporting group                       | Reporting group                           | Subject analysis set                       |  |
| Number of subjects analysed       | 19                                    | 19  | 38   |  |
| Units: Percentage of participants |                                       |   |  |  |
| number (confidence interval 95%)  | 23.2 (7.3 to<br>44.1)                 | 25 (7.8 to<br>47.2)                       | 24.3 (11.6 to<br>39.5)                     |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Overall Survival (OS) for PF-05212384**

|                 |  |
|-----------------|--|
| End point title | Overall Survival (OS) for PF-05212384 <sup>[7]</sup> |
|-----------------|--|

**End point description:**

OS is defined as the time from the date of Cycle 1 Day 1 to the date of death.

Survival analysis was not performed as the study was terminated early. No data are available because data were not collected. The LIC reporting arm were not a part of the per protocol analysis set for summarizing response.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

12 months

**Notes:**

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint has no statistical analysis.

| End point values                  | PF-05212384<br>154 mg (PI3K<br>Basal) | PF-05212384<br>154 mg (PI3K<br>Activated) | PF-05212384<br>(PI3K Basal +<br>Activated) |  |
|-----------------------------------|---------------------------------------|---|--|--|
| Subject group type                | Reporting group                       | Reporting group                           | Subject analysis set                       |  |
| Number of subjects analysed       | 0 <sup>[8]</sup>                      | 0 <sup>[9]</sup>                          | 0 <sup>[10]</sup>                          |  |
| Units: Percentage of participants |                                       |   |  |  |

Notes:

[8] - Survival analysis was not performed as the study was terminated early. No data are available.

[9] - Survival analysis was not performed as the study was terminated early. No data are available.

[10] - Survival analysis was not performed as the study was terminated early. No data are available.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Level of each pharmacodynamic parameter at specified timepoints- Glucose (mg/dL)

|                 |  |
|-----------------|--|
| End point title | Level of each pharmacodynamic parameter at specified timepoints- Glucose (mg/dL) <sup>[11]</sup> |
|-----------------|--|

End point description:

PD biomarkers are measured at screening (baseline) and multiple time points post baseline. Baseline is defined as the last measurement prior to dosing, which is the measurement at screening or the cycle 1 day 1 pre-dose measurement if collected. Subjects were analyzed on PD analysis set which consisted of all enrolled patients who started treatment and had a baseline as well as at least one post-baseline measurement for at least one PD biomarker. The PD biomarkers include serum glucose, insulin, HbA1c, cholesterol, and triglycerides.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day -3) and Cycle1 to Cycle 5 where each cycle consist of 28 days

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint has no statistical analysis.

| End point values                     | PF-05212384<br>154 mg (PI3K<br>Basal) | PF-05212384<br>154 mg (PI3K<br>Activated) | PF-05212384<br>(PI3K Basal +<br>Activated) |  |
|--------------------------------------|---------------------------------------|---|--|--|
| Subject group type                   | Reporting group                       | Reporting group                           | Subject analysis set                       |  |
| Number of subjects analysed          | 18                                    | 18  | 36   |  |
| Units: Glucose (mg/dL)               |                                       |   |  |  |
| arithmetic mean (standard deviation) |                                       |   |  |  |
| Baseline                             | 98.5 (± 12.76)                        | 101.7 (± 26.56)                           | 100.1 (± 20.6)                             |  |
| Cycle 1 Day 15 (n=18,17,35)          | 105.3 (± 18.44)                       | 117.2 (± 61.04)                           | 111.1 (± 44.26)                            |  |
| Cycle 1 Day 22 (n=2,1,3)             | 103 (± 19.31)                         | 114 (± 39.42)                             | 108.7 (± 15.19)                            |  |
| Cycle 2 Day 1 (n=17,14,31)           | 103.7 (± 19.31)                       | 114 (± 39.42)                             | 108.3 (± 29.99)                            |  |
| Cycle 2 Day 15 (n=17,8,25)           | 104.8 (± 13.94)                       | 106.4 (± 19.36)                           | 105.3 (± 15.47)                            |  |
| Cycle 3 Day 1 (n=14,10,24)           | 100.6 (± 16.29)                       | 125.9 (± 74.5)                            | 111.1 (± 49.85)                            |  |
| Cycle 4 Day 1 (n=12,7,19)            | 96.3 (± 10.4)                         | 98.9 (± 10.2)                             | 97.3 (± 10.12)                             |  |
| Cycle 5 Day 1 (n=9,4,13)             | 103.2 (± 15.17)                       | 112.2 (± 24.37)                           | 106 (± 17.9)                               |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Level of each pharmacodynamic parameter at specified timepoints- Insulin (UIU/mL)

|                 |   |
|-----------------|---|
| End point title | Level of each pharmacodynamic parameter at specified timepoints- Insulin (UIU/mL) <sup>[12]</sup> |
|-----------------|---|

End point description:

PD biomarkers are measured at screening (baseline) and multiple time points post baseline. Baseline is defined as the last measurement prior to dosing, which is the measurement at screening or the cycle 1 day 1 pre-dose measurement if collected. Subjects were analyzed on PD analysis set which consisted of all enrolled patients who started treatment and had a baseline as well as at least one post-baseline measurement for at least one PD biomarker. The PD biomarkers include serum glucose, insulin, HbA1c, cholesterol, and triglycerides.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day -3) and Cycle1 to Cycle 5 where each cycle consist of 28 days

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint has no statistical analysis.

| End point values                     | PF-05212384<br>154 mg (PI3K<br>Basal) | PF-05212384<br>154 mg (PI3K<br>Activated) | PF-05212384<br>(PI3K Basal +<br>Activated) |  |
|--------------------------------------|---------------------------------------|---|--|--|
| Subject group type                   | Reporting group                       | Reporting group                           | Subject analysis set                       |  |
| Number of subjects analysed          | 17                                    | 14  | 31   |  |
| Units: Insulin (UIU/mL)              |                                       |   |  |  |
| arithmetic mean (standard deviation) |                                       |   |  |  |
| Baseline                             | 15.2 (± 12.68)                        | 14.4 (± 7.03)                             | 14.8 (± 10.36)                             |  |
| Cycle 1 Day 15 (n=16,12,28)          | 23.6 (± 14.69)                        | 35.9 (± 37.05)                            | 28.9 (± 26.79)                             |  |
| Cycle 1 Day 22 (n=2,1,3)             | 57.6 (± 51.18)                        | 29.1 (± 0)                                | 48.1 (± 39.75)                             |  |
| Cycle 2 Day 1 (n=17,10,27)           | 30.3 (± 28.92)                        | 28.9 (± 27.85)                            | 29.8 (± 27.99)                             |  |
| Cycle 2 Day 15 (n=14,6,20)           | 28.2 (± 29.56)                        | 21.9 (± 10.49)                            | 26.3 (± 25.21)                             |  |
| Cycle 3 Day 1 (n=13,9,22)            | 20.7 (± 13.65)                        | 35.1 (± 38.66)                            | 26.6 (± 26.99)                             |  |
| Cycle 4 Day 1 (n=11,6,17)            | 17.1 (± 10.04)                        | 24.8 (± 32.32)                            | 19.8 (± 20.1)                              |  |
| Cycle 5 Day 1 (n=7,4,11)             | 17 (± 15.56)                          | 15.7 (± 6.2)                              | 16.5 (± 12.54)                             |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of participants in each treatment arm with gene and/or protein expression biomarkers in biopsied tumor tissue- Summary of Biomarkers - Molecular Profiling Tumor Analysis Set: Stathmin H Score (N)

|                 |  |
|-----------------|--|
| End point title | Percentage of participants in each treatment arm with gene and/or protein expression biomarkers in biopsied tumor tissue- Summary of Biomarkers - Molecular Profiling Tumor Analysis Set: Stathmin H Score (N) <sup>[13]</sup> |
|-----------------|--|

End point description:

Gene and/or protein expression biomarkers in biopsied tumor tissue relating to PI3K and/or mTOR pathway activation, such as PIK3CA and PIK3R1 mutations, PTEN protein levels, and PIK3CA gene

amplification were to be assessed.

Subjects were analyzed as the molecular profiling tumor analysis set was defined as all enrolled patients who started treatment and had baseline tumor tissues (archived paraffin block or unstained slides or fresh tumor tissue sample) successfully analyzed for at least one of the biomarkers.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and Cycle1 to Cycle 5 where each cycle consist of 28 days

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint has no statistical analysis.

|                                      |                                       |   |  |  |
|--------------------------------------|---------------------------------------|---|--|--|
| <b>End point values</b>              | PF-05212384<br>154 mg (PI3K<br>Basal) | PF-05212384<br>154 mg (PI3K<br>Activated) | PF-05212384<br>(PI3K Basal +<br>Activated) |  |
| Subject group type                   | Reporting group                       | Reporting group                           | Subject analysis set                       |  |
| Number of subjects analysed          | 19                                    | 19  | 40   |  |
| Units: Score                         |                                       |   |  |  |
| arithmetic mean (standard deviation) | 96.4 (± 33.76)                        | 201.3 (±<br>34.87)                        | 146.2 (± 62.9)                             |  |

## Statistical analyses

No statistical analyses for this end point

**Secondary: Percentage of participants in each treatment arm with gene and/or protein expression biomarkers- PIK3CA Amplification, KRAS Mutation P/N, KRAS Mutation OBSV, PTEN Stroma Manual Score, PTEN Tumor Manual Score, KRAS SCC and Stathmin H/L,Tissue.**

|                 |  |
|-----------------|--|
| End point title | Percentage of participants in each treatment arm with gene and/or protein expression biomarkers- PIK3CA Amplification, KRAS Mutation P/N, KRAS Mutation OBSV, PTEN Stroma Manual Score, PTEN Tumor Manual Score, KRAS SCC and Stathmin H/L,Tissue. <sup>[14]</sup> |
|-----------------|--|

End point description:

Gene and/or protein expression biomarkers in biopsied tumor tissue relating to PI3K and/or mTOR pathway activation, such as PIK3CA and PIK3R1 mutations, PTEN protein levels, and PIK3CA gene amplification were to be assessed.

Subjects were analyzed as the molecular profiling tumor analysis set was defined as all enrolled patients who started treatment and had baseline tumor tissues (archived paraffin block or unstained slides or fresh tumor tissue sample) successfully analyzed for at least one of the biomarkers.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and Cycle 1 to Cycle 5 where each cycle consist of 28 days

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint has no statistical analysis.

| End point values                                   | PF-05212384<br>154 mg (PI3K<br>Basal) | PF-05212384<br>154 mg (PI3K<br>Activated) | PF-05212384<br>(PI3K Basal +<br>Activated) |  |
|--|---------------------------------------|---|--|--|
| Subject group type                                 | Reporting group                       | Reporting group                           | Subject analysis set                       |  |
| Number of subjects analysed                        | 20 <sup>[15]</sup>                    | 20 <sup>[16]</sup>                        | 40   |  |
| Units: Percentage                                  |                                       |   |  |  |
| number (not applicable)                            |                                       |   |  |  |
| PIK3CA Amplification, Amplified<br>(n=17,15,32)    | 5.9                                   | 6.7                                       | 6.3  |  |
| PIK3CA Amplification, Nonamplified<br>(n=17,15,32) | 94.1                                  | 93.3                                      | 93.8                                       |  |
| KRAS Mutation, Positive (n=21,18,39)               | 19                                    | 5.6                                       | 12.8                                       |  |
| KRAS Mutation, Negative (n=21,18,39)               | 81                                    | 94.4                                      | 87.2                                       |  |
| KRAS Mutation OBSV, Gly12Asp<br>(n=4,1,5)          | 25                                    | 100                                       | 40   |  |
| KRAS Mutation OBSV, Gly12Cys<br>(n=4,1,5)          | 25                                    | 0   | 20   |  |
| KRAS Mutation OBSV, Gly12Val<br>(n=4,1,5)          | 50                                    | 0   | 40   |  |
| PTEN Stroma Manual Score, 1+<br>(n=21,19,40)       | 4.8                                   | 0   | 2.5  |  |
| PTEN Stroma Manual Score, 2+<br>(n=21,19,40)       | 28.6                                  | 26.3                                      | 27.5                                       |  |
| PTEN Stroma Manual Score, 3+<br>(n=21,19,40)       | 66.7                                  | 73.7                                      | 70   |  |
| PTEN Tumor Manual Score, 0<br>(n=21,19,40)         | 23.8                                  | 21.1                                      | 22.5                                       |  |
| PTEN Tumor Manual Score, 1+<br>(n=21,19,40)        | 38.1                                  | 31.6                                      | 35   |  |
| PTEN Tumor Manual Score, 2+<br>(n=21,19,40)        | 38.1                                  | 47.4                                      | 42.5                                       |  |
| KRAS SCC, Acceptable (n=21,18,39)                  | 100                                   | 100                                       | 100  |  |
| Sthathmin H/L,Tissue, High (n=21,19,40)            | 0                                     | 100                                       | 47.5                                       |  |
| Sthathmin H/L,Tissue, Low (n=21,19,40)             | 100                                   | 0   | 52.5                                       |  |

Notes:

[15] - N=21

One subject had the stathmin status changed and was categorized under Basal.

[16] - N= 19

One subject had their stathmin status changed and was categorized under Basal.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Area under the serum concentration time profile from time zero extrapolated to infinity (AUCinf) of PF-05212384 at each specified time points.

|                 |  |
|-----------------|--|
| End point title | Area under the serum concentration time profile from time zero extrapolated to infinity (AUCinf) of PF-05212384 at each specified time points. <sup>[17]</sup> |
|-----------------|--|

End point description:

AUCinf of PF-05212384 at each specified time points. Subjects were analyzed on PK parameter analysis set which was defined as all treated patients who had at least one of the PK parameters of interest estimated.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Day 1 until 35 days post last dose

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint has no statistical analysis.

| End point values                                    | PF-05212384<br>154 mg (PI3K<br>Basal) | PF-05212384<br>154 mg (PI3K<br>Activated) |  |  |
|---|---------------------------------------|---|--|--|
| Subject group type                                  | Reporting group                       | Reporting group                           |  |  |
| Number of subjects analysed                         | 19                                    | 15  |  |  |
| Units: ng.hr/mL                                     |                                       |   |  |  |
| geometric mean (geometric coefficient of variation) | 15280 ( $\pm$ 24)                     | 14870 ( $\pm$ 40)                         |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Area under the serum concentration time profile from time zero to the time of the last quantifiable concentration (AUClast) of PF-05212384 at each specified time points.

|                 |   |
|-----------------|---|
| End point title | Area under the serum concentration time profile from time zero to the time of the last quantifiable concentration (AUClast) of PF-05212384 at each specified time points. <sup>[18]</sup> |
|-----------------|---|

End point description:

AUClast of PF-05212384 at each specified time points.

Subjects were analyzed on PK parameter analysis set which was defined as all treated patients who had at least one of the PK parameters of interest estimated.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Day 1 until 35 days post last dose

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint has no statistical analysis.

| End point values                                    | PF-05212384<br>154 mg (PI3K<br>Basal) | PF-05212384<br>154 mg (PI3K<br>Activated) |  |  |
|---|---------------------------------------|---|--|--|
| Subject group type                                  | Reporting group                       | Reporting group                           |  |  |
| Number of subjects analysed                         | 19                                    | 15  |  |  |
| Units: ng.hr/mL                                     |                                       |   |  |  |
| geometric mean (geometric coefficient of variation) | 15080 ( $\pm$ 24)                     | 15890 ( $\pm$ 52)                         |  |  |

## Statistical analyses

No statistical analyses for this end point

**Secondary: Maximum plasma concentration (C<sub>max</sub>) of PF-05212384 at each specified time points.**

|                 |  |
|-----------------|--|
| End point title | Maximum plasma concentration (C <sub>max</sub> ) of PF-05212384 at each specified time points. <sup>[19]</sup> |
|-----------------|--|

End point description:

C<sub>max</sub> of PF-05212384 at each specified time points.

Subjects were analyzed on PK parameter analysis set which was defined as all treated patients who had at least one of the PK parameters of interest estimated.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Day 1 until 35 days post last dose

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint has no statistical analysis.

|   |                                       |   |  |  |
|---|---------------------------------------|---|--|--|
| <b>End point values</b>                             | PF-05212384<br>154 mg (PI3K<br>Basal) | PF-05212384<br>154 mg (PI3K<br>Activated) |  |  |
| Subject group type                                  | Reporting group                       | Reporting group                           |  |  |
| Number of subjects analysed                         | 19                                    | 15  |  |  |
| Units: ng/mL  |                                       |   |  |  |
| geometric mean (geometric coefficient of variation) | 9078 (± 36)                           | 7057 (± 84)                               |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Terminal elimination half life (t<sub>1/2</sub>) of PF-05212384 at each specified time points.**

|                 |  |
|-----------------|--|
| End point title | Terminal elimination half life (t <sub>1/2</sub> ) of PF-05212384 at each specified time points. <sup>[20]</sup> |
|-----------------|--|

End point description:

t<sub>1/2</sub> of PF-05212384 at each specified time points.

Subjects were analyzed on PK parameter analysis set which was defined as all treated patients who had at least one of the PK parameters of interest estimated.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Day 1 until 35 days post last dose

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint has no statistical analysis.



|                                      |                                       |   |  |  |
|--------------------------------------|---------------------------------------|---|--|--|
| <b>End point values</b>              | PF-05212384<br>154 mg (PI3K<br>Basal) | PF-05212384<br>154 mg (PI3K<br>Activated) |  |  |
| Subject group type                   | Reporting group                       | Reporting group                           |  |  |
| Number of subjects analysed          | 19                                    | 15  |  |  |
| Units: hr                            |                                       |   |  |  |
| arithmetic mean (standard deviation) | 35.02 (± 5.32)                        | 34.09 (± 8.87)                            |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Time for Cmax (Tmax) of PF-05212384 at each specified time points.

|                 |  |
|-----------------|--|
| End point title | Time for Cmax (Tmax) of PF-05212384 at each specified time points. <sup>[21]</sup> |
|-----------------|--|

End point description:

Tmax of PF-05212384 at each specified time points.

Subjects were analyzed on PK parameter analysis set which was defined as all treated patients who had at least one of the PK parameters of interest estimated.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Day 1 until 35 days post last dose

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint has no statistical analysis.

|                               |                                       |   |  |  |
|-------------------------------|---------------------------------------|---|--|--|
| <b>End point values</b>       | PF-05212384<br>154 mg (PI3K<br>Basal) | PF-05212384<br>154 mg (PI3K<br>Activated) |  |  |
| Subject group type            | Reporting group                       | Reporting group                           |  |  |
| Number of subjects analysed   | 19                                    | 15  |  |  |
| Units: hr                     |                                       |   |  |  |
| median (full range (min-max)) | 0.525 (0.5 to<br>1.07)                | 0.65 (0.5 to<br>1.08)                     |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Clearance (CL) of PF-05212384 at each specified time points.

|                 |  |
|-----------------|--|
| End point title | Clearance (CL) of PF-05212384 at each specified time |
|-----------------|--|

End point description:

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Day 1 until 35 days post last dose

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint has no statistical analysis.

| End point values                                       | PF-05212384<br>154 mg (PI3K<br>Basal) | PF-05212384<br>154 mg (PI3K<br>Activated) |  |  |
|--|---------------------------------------|---|--|--|
| Subject group type                                     | Reporting group                       | Reporting group                           |  |  |
| Number of subjects analysed                            | 19                                    | 15  |  |  |
| Units: L/hr  |                                       |   |  |  |
| geometric mean (geometric coefficient<br>of variation) | 10.09 (± 24)                          | 10.36 (± 40)                              |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Steady state volume of distribution (Vss) of PF-05212384 at each specified time points.

|                 |   |
|-----------------|---|
| End point title | Steady state volume of distribution (Vss) of PF-05212384 at each specified time points. <sup>[23]</sup> |
|-----------------|---|

End point description:

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 1 to Day 5

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint has no statistical analysis.

| End point values                                       | PF-05212384<br>154 mg (PI3K<br>Basal) | PF-05212384<br>154 mg (PI3K<br>Activated) |  |  |
|--|---------------------------------------|---|--|--|
| Subject group type                                     | Reporting group                       | Reporting group                           |  |  |
| Number of subjects analysed                            | 19                                    | 15  |  |  |
| Units: Litres  |                                       |   |  |  |
| geometric mean (geometric coefficient<br>of variation) | 165.6 (± 32)                          | 174.9 (± 57)                              |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Summary of treatment-emergent adverse events (TEAEs) - all causalities

|                 |  |
|-----------------|--|
| End point title | Summary of treatment-emergent adverse events (TEAEs) - all causalities <sup>[24]</sup> |
|-----------------|--|

End point description:

Safety of participants in terms of TEAEs.

End point type Secondary

End point timeframe:

From baseline (-3 days) until 35 days post last dose

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint has no statistical analysis.

| End point values                                   | PF-05212384<br>154 mg (PI3K<br>Basal) | PF-05212384<br>154 mg (PI3K<br>Activated) | PF-05212384<br>(PI3K Basal +<br>Activated) |  |
|--|---------------------------------------|---|--|--|
| Subject group type                                 | Reporting group                       | Reporting group                           | Subject analysis set                       |  |
| Number of subjects analysed                        | 2                                     | 1   | 3  |  |
| Units: Participants                                |                                       |   |  |  |
| Number of Adverse Events (AEs)                     | 10                                    | 6   | 16   |  |
| Participants with AEs                              | 2                                     | 1   | 3  |  |
| Participants with Serious Adverse Events<br>(SAEs) | 0                                     | 0   | 0  |  |
| Participants with Grade 3 or Grade 4<br>AEs        | 1                                     | 1   | 2  |  |
| Participants with Grade 5 AEs                      | 0                                     | 0   | 0  |  |
| Permanently Discontinued due to AEs                | 1                                     | 1   | 2  |  |
| Dose Reduced due to AEs                            | 0                                     | 0   | 0  |  |
| Temporary Discontinuations due to AEs              | 1                                     | 1   | 2  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Summary of treatment-related TEAEs

End point title Summary of treatment-related TEAEs<sup>[25]</sup>

End point description:

Safety of subject in terms of number of participants with treatment related AEs.

End point type Secondary

End point timeframe:

From baseline (-3 days) until 35 days post last dose

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint has no statistical analysis.

| End point values            | PF-05212384<br>154 mg (PI3K<br>Basal) | PF-05212384<br>154 mg (PI3K<br>Activated) | PF-05212384<br>(PI3K Basal +<br>Activated) |  |
|-----------------------------|---------------------------------------|---|--|--|
| Subject group type          | Reporting group                       | Reporting group                           | Subject analysis set                       |  |
| Number of subjects analysed | 2                                     | 1   | 3  |  |
| Units: Participants         |                                       |   |  |  |
| Number of AEs               | 9                                     | 5   | 14   |  |

|  |   |   |   |  |
|--|---|---|---|--|
| Participants with AEs                    | 2 | 1 | 3 |  |
| Participants with SAEs                   | 0 | 0 | 0 |  |
| Participants with Grade 3 or Grade 4 AEs | 1 | 1 | 2 |  |
| Participants with Grade 5 AEs            | 0 | 0 | 0 |  |
| Permanently Discontinued due to AEs      | 1 | 1 | 2 |  |
| Dose Reduced due to AEs                  | 0 | 0 | 0 |  |
| Temporary Discontinuations due to AEs    | 1 | 1 | 2 |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Level of each pharmacodynamic parameter at specified timepoints- Glycosylated Hemoglobin (HbA1c)

|                 |  |
|-----------------|--|
| End point title | Level of each pharmacodynamic parameter at specified timepoints- Glycosylated Hemoglobin (HbA1c) <sup>[26]</sup> |
|-----------------|--|

End point description:

PD biomarkers are measured at screening (baseline) and multiple time points post baseline. Baseline is defined as the last measurement prior to dosing, which is the measurement at screening or the cycle 1 day 1 pre-dose measurement if collected.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day -3) and Cycle1 to Cycle 5 where each cycle consist of 28 days

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint has no statistical analysis.

| End point values                     | PF-05212384<br>154 mg (PI3K<br>Basal) | PF-05212384<br>154 mg (PI3K<br>Activated) | PF-05212384<br>(PI3K Basal +<br>Activated) |  |
|--------------------------------------|---------------------------------------|---|--|--|
| Subject group type                   | Reporting group                       | Reporting group                           | Subject analysis set                       |  |
| Number of subjects analysed          | 18                                    | 18  | 36   |  |
| Units: HbA1c                         |                                       |   |  |  |
| arithmetic mean (standard deviation) |                                       |   |  |  |
| Baseline (n=15,14,29)                | 7.8 (± 8.58)                          | 7.5 (± 6.15)                              | 7.7 (± 7.37)                               |  |
| Cycle 1 Day 15 (n=4,2,6)             | 14.7 (± 19)                           | 7.1 (± 1.34)                              | 12.2 (± 15.25)                             |  |
| Cycle 2 Day 1 (n=14,11,25)           | 1.08 (± 0.056)                        | 1.13 (± 0.088)                            | 1.1 (± 0.075)                              |  |
| Cycle 2 Day 15 (n=3,0,3)             | 6.7 (± 0.71)                          | 0 (± 0)                                   | 6.7 (± 0.71)                               |  |
| Cycle 3 Day 1 (n=10,4,14)            | 6 (± 0.78)                            | 7.3 (± 1.7)                               | 6.4 (± 1.19)                               |  |
| Cycle 4 Day 1 (n=12,7,19)            | 8.9 (± 10.13)                         | 6.9 (± 1.05)                              | 8.2 (± 8.01)                               |  |
| Cycle 5 Day 1 (n=8,2,10)             | 5.9 (± 0.89)                          | 31.5 (± 36.06)                            | 11 (± 16.17)                               |  |

## Statistical analyses

No statistical analyses for this end point

**Secondary: Level of each pharmacodynamic parameter at specified timepoints- Cholesterol (mg/dL)**

|                 |  |
|-----------------|--|
| End point title | Level of each pharmacodynamic parameter at specified timepoints- Cholesterol (mg/dL) <sup>[27]</sup> |
|-----------------|--|

End point description:

PD biomarkers are measured at screening (baseline) and multiple time points post baseline. Baseline is defined as the last measurement prior to dosing, which is the measurement at screening or the cycle 1 day 1 pre-dose measurement if collected.

Subjects were analyzed on PD analysis set which consisted of all enrolled patients who started treatment and had a baseline as well as at least one post-baseline measurement for at least one PD biomarker.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day -3) and Cycle 1 to Cycle 3 where each cycle consist of 28 days

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint has no statistical analysis.

| End point values                     | PF-05212384<br>154 mg (PI3K<br>Basal) | PF-05212384<br>154 mg (PI3K<br>Activated) | PF-05212384<br>(PI3K Basal +<br>Activated) |  |
|--------------------------------------|---------------------------------------|---|--|--|
| Subject group type                   | Reporting group                       | Reporting group                           | Subject analysis set                       |  |
| Number of subjects analysed          | 18                                    | 18  | 36   |  |
| Units: Cholesterol (mg/dL)           |                                       |   |  |  |
| arithmetic mean (standard deviation) |                                       |   |  |  |
| Baseline (n=11,4,15)                 | 213 (± 54.48)                         | 186.5 (± 52.43)                           | 205.9 (± 53.45)                            |  |
| Cycle 1 Day 28 (n=15,7,22)           | 214.9 (± 49.15)                       | 161.6 (± 86.51)                           | 198 (± 66.28)                              |  |
| Cycle 2 Day 22 (n=16,6,22)           | 229.8 (± 44.31)                       | 127.9 (± 108.69)                          | 202 (± 79.83)                              |  |
| Cycle 3 Day 28 (n=11,4,15)           | 230.5 (± 48.63)                       | 137.6 (± 107.02)                          | 205.7 (± 77.15)                            |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Level of each pharmacodynamic parameter at specified timepoints- Triglycerides (mg/dL)**

|                 |  |
|-----------------|--|
| End point title | Level of each pharmacodynamic parameter at specified timepoints- Triglycerides (mg/dL) <sup>[28]</sup> |
|-----------------|--|

End point description:

PD biomarkers are measured at screening (baseline) and multiple time points post baseline. Baseline is defined as the last measurement prior to dosing, which is the measurement at screening or the cycle 1 day 1 pre-dose measurement if collected.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day -3) and Cycle1 to Cycle 3 where each cycle consist of 28 days

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint has no statistical analysis.

| End point values                     | PF-05212384<br>154 mg (PI3K<br>Basal) | PF-05212384<br>154 mg (PI3K<br>Activated) | PF-05212384<br>(PI3K Basal +<br>Activated) |  |
|--------------------------------------|---------------------------------------|---|--|--|
| Subject group type                   | Reporting group                       | Reporting group                           | Subject analysis set                       |  |
| Number of subjects analysed          | 18                                    | 18  | 36   |  |
| Units: Triglycerides (mg/dL)         |                                       |   |  |  |
| arithmetic mean (standard deviation) |                                       |   |  |  |
| Baseline (n=11,4,15)                 | 104.2 (±<br>40.95)                    | 133.4 (±<br>25.75)                        | 112 (± 38.96)                              |  |
| Cycle 1 Day 28 (n=15,7,22)           | 136.9 (±<br>70.03)                    | 134.5 (±<br>57.21)                        | 136.1 (±<br>64.85)                         |  |
| Cycle 2 Day 28 (n=16,6,22)           | 133.2 (± 71.4)                        | 117.1 (±<br>62.77)                        | 128.8 (±<br>68.07)                         |  |
| Cycle 3 Day 28 (n=10,4,14)           | 119.9 (±<br>64.22)                    | 130.4 (±<br>58.01)                        | 122.9 (±<br>60.47)                         |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Maximum of treatment duration (i.e., 21 to 169 days for the PF 04691502 [PI3K basal and activated], 29 to 345 days for PF 05212384 PI3K basal and 1 to 400 days for PF 05212384 PI3K activated) + 28 days across all participants.

Adverse event reporting additional description:

All causality AEs and SAEs are included in this section. The same event may appear as both an AE and a SAE. However, what is presented are distinct events. An event may be categorized as serious in one participant and as nonserious in another participant, or one participant may have experienced both a serious and nonserious event during the study.

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 18.1   |

### Reporting groups

|                       |                               |
|-----------------------|-------------------------------|
| Reporting group title | PF-04691502 8 mg (PI3K Basal) |
|-----------------------|-------------------------------|

Reporting group description:

Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K basal). Participants self-administered PF-04691502 8 mg orally, QD until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death. Dose of the participants were reduced to 6 mg if they were on 8 mg dose.

|                       |                               |
|-----------------------|-------------------------------|
| Reporting group title | PF-04691502 6 mg (PI3K Basal) |
|-----------------------|-------------------------------|

Reporting group description:

Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K basal). Participants self-administered PF-04691502 6 mg orally, QD until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | PF-04691502 8 mg (PI3K Activated) |
|-----------------------|-----------------------------------|

Reporting group description:

Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K activated). Participants self-administered PF-04691502 8 mg orally, QD until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death. Dose of the participants were reduced to 6 mg if they were on 8 mg dose.

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | PF-04691502 6 mg (PI3K Activated) |
|-----------------------|-----------------------------------|

Reporting group description:

Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K activated). Participants self-administered PF-04691502 6 mg orally, QD until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.

|                       |                                 |
|-----------------------|---------------------------------|
| Reporting group title | PF-05212384 154 mg (PI3K Basal) |
|-----------------------|---------------------------------|

Reporting group description:

Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K basal). Participants received PF-05212384 154 mg by 30 minute infusion at the study site, QW (Quaque [Once Weekly]) until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.

|                       |   |
|-----------------------|---|
| Reporting group title | Lead-in-cohort (LIC) PF-04691502 (4 mg) |
|-----------------------|---|

Reporting group description:

Participants who were enrolled in the PF-04691502 LIC began dosing with PF-04691502 4 mg at least 4 days (but no more than 10 days) prior to Cycle 1 Day 1 and continued taking PF-05691502 until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.

|                       |                                     |
|-----------------------|-------------------------------------|
| Reporting group title | PF-05212384 154 mg (PI3K Activated) |
|-----------------------|-------------------------------------|

Reporting group description:

Eligible participants were categorized by PI3K pathway activation status (i.e. PI3K activated). Participants received PF-05212384 154 mg by 30 minute infusion at the study site, QW until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.

|   |                          |
|---|--------------------------|
| Reporting group title   | LIC PF-05212384 (89 mg)  |
| Reporting group description:  |                          |
| Participants who were enrolled in the PF-05212384 LIC began dosing with PF-05212384 89 mg at least 4 days (but no more than 10 days) prior to Cycle 1 Day 1 and continued taking PF-05212384 until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death.  |                          |
| Reporting group title   | LIC PF-05212384 (154 mg) |
| Reporting group description:  |                          |
| Participants who were enrolled in the PF-05212384 LIC began dosing with PF-05212384 154 mg at least 4 days (but no more than 10 days) prior to Cycle 1 Day 1 and continued taking PF-05212384 until they experienced unacceptable toxicity, disease progression, significant deviation, withdrawal of consent or death. |                          |

| <b>Serious adverse events</b>                                       | PF-04691502 8 mg<br>(PI3K Basal) | PF-04691502 6 mg<br>(PI3K Basal) | PF-04691502 8 mg<br>(PI3K Activated) |
|---|----------------------------------|----------------------------------|--------------------------------------|
| Total subjects affected by serious adverse events                   |                                  |                                  |                                      |
| subjects affected / exposed   | 3 / 5 (60.00%)                   | 1 / 1 (100.00%)                  | 7 / 9 (77.78%)                       |
| number of deaths (all causes)                                       | 3                                | 0                                | 6                                    |
| number of deaths resulting from adverse events                      | 0                                | 0                                | 1                                    |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                  |                                  |                                      |
| Gastric Cancer  |                                  |                                  |                                      |
| subjects affected / exposed   | 0 / 5 (0.00%)                    | 0 / 1 (0.00%)                    | 0 / 9 (0.00%)                        |
| occurrences causally related to treatment / all                     | 0 / 0                            | 0 / 0                            | 0 / 0                                |
| deaths causally related to treatment / all                          | 0 / 0                            | 0 / 0                            | 0 / 0                                |
| Vascular disorders  |                                  |                                  |                                      |
| Deep Vein Thrombosis  |                                  |                                  |                                      |
| subjects affected / exposed   | 0 / 5 (0.00%)                    | 0 / 1 (0.00%)                    | 0 / 9 (0.00%)                        |
| occurrences causally related to treatment / all                     | 0 / 0                            | 0 / 0                            | 0 / 0                                |
| deaths causally related to treatment / all                          | 0 / 0                            | 0 / 0                            | 0 / 0                                |
| General disorders and administration site conditions                |                                  |                                  |                                      |
| Chills  |                                  |                                  |                                      |
| subjects affected / exposed   | 0 / 5 (0.00%)                    | 0 / 1 (0.00%)                    | 0 / 9 (0.00%)                        |
| occurrences causally related to treatment / all                     | 0 / 0                            | 0 / 0                            | 0 / 0                                |
| deaths causally related to treatment / all                          | 0 / 0                            | 0 / 0                            | 0 / 0                                |
| Disease Progression   |                                  |                                  |                                      |
| subjects affected / exposed   | 0 / 5 (0.00%)                    | 0 / 1 (0.00%)                    | 0 / 9 (0.00%)                        |
| occurrences causally related to treatment / all                     | 0 / 0                            | 0 / 0                            | 0 / 0                                |
| deaths causally related to treatment / all                          | 0 / 0                            | 0 / 0                            | 0 / 0                                |
| Respiratory, thoracic and mediastinal disorders                     |                                  |                                  |                                      |



|   |                |               |                |
|---|----------------|---------------|----------------|
| Acute Respiratory Distress Syndrome             |                |               |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Pneumonia Aspiration                            |                |               |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 1 / 1          |
| Pneumonitis                                     |                |               |                |
| subjects affected / exposed                     | 2 / 5 (40.00%) | 0 / 1 (0.00%) | 2 / 9 (22.22%) |
| occurrences causally related to treatment / all | 2 / 2          | 0 / 0         | 2 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Pneumothorax Spontaneous                        |                |               |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Pulmonary Embolism                              |                |               |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Investigations                                  |                |               |                |
| Lymphocyte Count Decreased                      |                |               |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Cardiac disorders                               |                |               |                |
| Cardiac Failure                                 |                |               |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Nervous system disorders                        |                |               |                |
| Cerebrovascular Accident                        |                |               |                |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| <b>Gastrointestinal disorders</b>               |                |                 |                |
| <b>Diarrhoea</b>                                |                |                 |                |
| subjects affected / exposed                     | 1 / 5 (20.00%) | 0 / 1 (0.00%)   | 2 / 9 (22.22%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0           | 2 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| <b>Large Intestinal Obstruction</b>             |                |                 |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| <b>Nausea</b>                                   |                |                 |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| <b>Oral Pain</b>                                |                |                 |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 1 / 1 (100.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| <b>Stomatitis</b>                               |                |                 |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 1 / 1 (100.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1           | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| <b>Vomiting</b>                                 |                |                 |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| <b>Skin and subcutaneous tissue disorders</b>   |                |                 |                |
| <b>Dermatitis</b>                               |                |                 |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| <b>Urticaria</b>                                |                |                 |                |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 1 / 1 (100.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Renal and urinary disorders                     |                |                 |                |
| Acute Kidney Injury                             |                |                 |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Urinary Tract Obstruction                       |                |                 |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Musculoskeletal and connective tissue disorders |                |                 |                |
| Arthralgia                                      |                |                 |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Fistula   |                |                 |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Infections and infestations                     |                |                 |                |
| Lung Infection                                  |                |                 |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Pneumocystis Jirovecii Pneumonia                |                |                 |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Pneumonia                                       |                |                 |                |
| subjects affected / exposed                     | 1 / 5 (20.00%) | 0 / 1 (0.00%)   | 2 / 9 (22.22%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0           | 2 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |

|   |               |               |                |
|---|---------------|---------------|----------------|
| Pyelonephritis                                  |               |               |                |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Skin Infection                                  |               |               |                |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Urinary Tract Infection                         |               |               |                |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Metabolism and nutrition disorders              |               |               |                |
| Diabetic Ketoacidosis                           |               |               |                |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Hyperglycaemia                                  |               |               |                |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |

| <b>Serious adverse events</b>                                       | PF-04691502 6 mg<br>(PI3K Activated) | PF-05212384 154<br>mg (PI3K Basal) | Lead-in-cohort (LIC)<br>PF-04691502 (4 mg) |
|---|--------------------------------------|------------------------------------|--|
| Total subjects affected by serious adverse events                   |                                      |                                    |  |
| subjects affected / exposed   | 1 / 3 (33.33%)                       | 3 / 21 (14.29%)                    | 1 / 3 (33.33%)                             |
| number of deaths (all causes)                                       | 0                                    | 8                                  | 0  |
| number of deaths resulting from adverse events                      | 0                                    | 0                                  | 0  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                      |                                    |  |
| Gastric Cancer  |                                      |                                    |  |
| subjects affected / exposed   | 0 / 3 (0.00%)                        | 0 / 21 (0.00%)                     | 0 / 3 (0.00%)                              |
| occurrences causally related to treatment / all                     | 0 / 0                                | 0 / 0                              | 0 / 0                                      |
| deaths causally related to treatment / all                          | 0 / 0                                | 0 / 0                              | 0 / 0                                      |
| Vascular disorders  |                                      |                                    |  |
| Deep Vein Thrombosis  |                                      |                                    |  |

|  |                |                |               |
|--|----------------|----------------|---------------|
| subjects affected / exposed                          | 0 / 3 (0.00%)  | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0         |
| General disorders and administration site conditions |                |                |               |
| Chills   |                |                |               |
| subjects affected / exposed                          | 0 / 3 (0.00%)  | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0         |
| Disease Progression                                  |                |                |               |
| subjects affected / exposed                          | 0 / 3 (0.00%)  | 1 / 21 (4.76%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 1          | 0 / 0         |
| Respiratory, thoracic and mediastinal disorders      |                |                |               |
| Acute Respiratory Distress Syndrome                  |                |                |               |
| subjects affected / exposed                          | 0 / 3 (0.00%)  | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0         |
| Pneumonia Aspiration                                 |                |                |               |
| subjects affected / exposed                          | 0 / 3 (0.00%)  | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0         |
| Pneumonitis  |                |                |               |
| subjects affected / exposed                          | 0 / 3 (0.00%)  | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0         |
| Pneumothorax Spontaneous                             |                |                |               |
| subjects affected / exposed                          | 1 / 3 (33.33%) | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all      | 1 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0         |
| Pulmonary Embolism                                   |                |                |               |
| subjects affected / exposed                          | 0 / 3 (0.00%)  | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0         |

|   |               |                |                |
|---|---------------|----------------|----------------|
| Investigations                                  |               |                |                |
| Lymphocyte Count Decreased                      |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 1 / 3 (33.33%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 7 / 7          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Cardiac disorders                               |               |                |                |
| Cardiac Failure                                 |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Nervous system disorders                        |               |                |                |
| Cerebrovascular Accident                        |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                      |               |                |                |
| Diarrhoea                                       |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Large Intestinal Obstruction                    |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Nausea  |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Oral Pain                                       |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Stomatitis                                      |               |                |                |

|   |               |                |               |
|---|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Vomiting  |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Skin and subcutaneous tissue disorders          |               |                |               |
| Dermatitis                                      |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Urticaria                                       |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Renal and urinary disorders                     |               |                |               |
| Acute Kidney Injury                             |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Urinary Tract Obstruction                       |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Musculoskeletal and connective tissue disorders |               |                |               |
| Arthralgia                                      |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Fistula   |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |

|   |                                 |                                  |                                  |
|---|---------------------------------|----------------------------------|----------------------------------|
| Infections and infestations<br>Lung Infection<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all               | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 21 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0  |
| Pneumocystis Jirovecii Pneumonia<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                            | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 21 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 3 (33.33%)<br>4 / 4<br>0 / 0 |
| Pneumonia<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all   | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 21 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0  |
| Pyelonephritis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all  | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 21 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0  |
| Skin Infection<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all  | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 21 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0  |
| Urinary Tract Infection<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                                     | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 21 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0  |
| Metabolism and nutrition disorders<br>Diabetic Ketoacidosis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 21 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0  |
| Hyperglycaemia<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all  | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 21 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 3 (0.00%)<br>0 / 0<br>0 / 0  |



| <b>Serious adverse events</b>                                       | PF-05212384 154 mg (PI3K Activated) | LIC PF-05212384 (89 mg) | LIC PF-05212384 (154 mg) |
|---|-------------------------------------|-------------------------|--------------------------|
| Total subjects affected by serious adverse events                   |                                     |                         |                          |
| subjects affected / exposed   | 10 / 19 (52.63%)                    | 0 / 3 (0.00%)           | 1 / 3 (33.33%)           |
| number of deaths (all causes)                                       | 11                                  | 1                       | 1                        |
| number of deaths resulting from adverse events                      | 0                                   | 0                       | 0                        |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                     |                         |                          |
| Gastric Cancer  |                                     |                         |                          |
| subjects affected / exposed   | 1 / 19 (5.26%)                      | 0 / 3 (0.00%)           | 0 / 3 (0.00%)            |
| occurrences causally related to treatment / all                     | 0 / 1                               | 0 / 0                   | 0 / 0                    |
| deaths causally related to treatment / all                          | 0 / 0                               | 0 / 0                   | 0 / 0                    |
| Vascular disorders  |                                     |                         |                          |
| Deep Vein Thrombosis  |                                     |                         |                          |
| subjects affected / exposed   | 1 / 19 (5.26%)                      | 0 / 3 (0.00%)           | 0 / 3 (0.00%)            |
| occurrences causally related to treatment / all                     | 0 / 1                               | 0 / 0                   | 0 / 0                    |
| deaths causally related to treatment / all                          | 0 / 0                               | 0 / 0                   | 0 / 0                    |
| General disorders and administration site conditions                |                                     |                         |                          |
| Chills  |                                     |                         |                          |
| subjects affected / exposed   | 1 / 19 (5.26%)                      | 0 / 3 (0.00%)           | 0 / 3 (0.00%)            |
| occurrences causally related to treatment / all                     | 1 / 1                               | 0 / 0                   | 0 / 0                    |
| deaths causally related to treatment / all                          | 0 / 0                               | 0 / 0                   | 0 / 0                    |
| Disease Progression   |                                     |                         |                          |
| subjects affected / exposed   | 2 / 19 (10.53%)                     | 0 / 3 (0.00%)           | 0 / 3 (0.00%)            |
| occurrences causally related to treatment / all                     | 0 / 2                               | 0 / 0                   | 0 / 0                    |
| deaths causally related to treatment / all                          | 0 / 2                               | 0 / 0                   | 0 / 0                    |
| Respiratory, thoracic and mediastinal disorders                     |                                     |                         |                          |
| Acute Respiratory Distress Syndrome                                 |                                     |                         |                          |
| subjects affected / exposed   | 0 / 19 (0.00%)                      | 0 / 3 (0.00%)           | 0 / 3 (0.00%)            |
| occurrences causally related to treatment / all                     | 0 / 0                               | 0 / 0                   | 0 / 0                    |
| deaths causally related to treatment / all                          | 0 / 0                               | 0 / 0                   | 0 / 0                    |
| Pneumonia Aspiration  |                                     |                         |                          |
| subjects affected / exposed   | 0 / 19 (0.00%)                      | 0 / 3 (0.00%)           | 0 / 3 (0.00%)            |
| occurrences causally related to treatment / all                     | 0 / 0                               | 0 / 0                   | 0 / 0                    |
| deaths causally related to treatment / all                          | 0 / 0                               | 0 / 0                   | 0 / 0                    |
| Pneumonitis   |                                     |                         |                          |

|   |                 |               |               |
|---|-----------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 19 (0.00%)  | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0         |
| Pneumothorax Spontaneous                        |                 |               |               |
| subjects affected / exposed                     | 0 / 19 (0.00%)  | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0         |
| Pulmonary Embolism                              |                 |               |               |
| subjects affected / exposed                     | 2 / 19 (10.53%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2           | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0         |
| Investigations                                  |                 |               |               |
| Lymphocyte Count Decreased                      |                 |               |               |
| subjects affected / exposed                     | 0 / 19 (0.00%)  | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0         |
| Cardiac disorders                               |                 |               |               |
| Cardiac Failure                                 |                 |               |               |
| subjects affected / exposed                     | 1 / 19 (5.26%)  | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0         |
| Nervous system disorders                        |                 |               |               |
| Cerebrovascular Accident                        |                 |               |               |
| subjects affected / exposed                     | 0 / 19 (0.00%)  | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0         |
| Gastrointestinal disorders                      |                 |               |               |
| Diarrhoea                                       |                 |               |               |
| subjects affected / exposed                     | 0 / 19 (0.00%)  | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0         |
| Large Intestinal Obstruction                    |                 |               |               |

|   |                |               |               |
|---|----------------|---------------|---------------|
| subjects affected / exposed                     | 1 / 19 (5.26%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 5          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Nausea  |                |               |               |
| subjects affected / exposed                     | 0 / 19 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Oral Pain                                       |                |               |               |
| subjects affected / exposed                     | 0 / 19 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Stomatitis                                      |                |               |               |
| subjects affected / exposed                     | 0 / 19 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Vomiting  |                |               |               |
| subjects affected / exposed                     | 0 / 19 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Skin and subcutaneous tissue disorders          |                |               |               |
| Dermatitis                                      |                |               |               |
| subjects affected / exposed                     | 0 / 19 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Urticaria                                       |                |               |               |
| subjects affected / exposed                     | 0 / 19 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Renal and urinary disorders                     |                |               |               |
| Acute Kidney Injury                             |                |               |               |
| subjects affected / exposed                     | 1 / 19 (5.26%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Urinary Tract Obstruction                       |                |               |               |

|  |                |               |                |
|--|----------------|---------------|----------------|
| subjects affected / exposed                            | 0 / 19 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences causally related to treatment / all        | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0         | 0 / 0          |
| <b>Musculoskeletal and connective tissue disorders</b> |                |               |                |
| Arthralgia   |                |               |                |
| subjects affected / exposed                            | 0 / 19 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences causally related to treatment / all        | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0         | 0 / 0          |
| Fistula  |                |               |                |
| subjects affected / exposed                            | 1 / 19 (5.26%) | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences causally related to treatment / all        | 0 / 1          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0         | 0 / 0          |
| <b>Infections and infestations</b>                     |                |               |                |
| Lung Infection   |                |               |                |
| subjects affected / exposed                            | 1 / 19 (5.26%) | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences causally related to treatment / all        | 0 / 1          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0         | 0 / 0          |
| Pneumocystis Jirovecii Pneumonia                       |                |               |                |
| subjects affected / exposed                            | 0 / 19 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences causally related to treatment / all        | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0         | 0 / 0          |
| Pneumonia  |                |               |                |
| subjects affected / exposed                            | 0 / 19 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences causally related to treatment / all        | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0         | 0 / 0          |
| Pyelonephritis   |                |               |                |
| subjects affected / exposed                            | 1 / 19 (5.26%) | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences causally related to treatment / all        | 0 / 1          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0         | 0 / 0          |
| Skin Infection   |                |               |                |
| subjects affected / exposed                            | 0 / 19 (0.00%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences causally related to treatment / all        | 0 / 0          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0         | 0 / 0          |

|   |                 |               |               |
|---|-----------------|---------------|---------------|
| Urinary Tract Infection                         |                 |               |               |
| subjects affected / exposed                     | 2 / 19 (10.53%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0         |
| Metabolism and nutrition disorders              |                 |               |               |
| Diabetic Ketoacidosis                           |                 |               |               |
| subjects affected / exposed                     | 0 / 19 (0.00%)  | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0         |
| Hyperglycaemia                                  |                 |               |               |
| subjects affected / exposed                     | 0 / 19 (0.00%)  | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0         |

Frequency threshold for reporting non-serious adverse events: 0 %

| <b>Non-serious adverse events</b>                                   | PF-04691502 8 mg<br>(PI3K Basal) | PF-04691502 6 mg<br>(PI3K Basal) | PF-04691502 8 mg<br>(PI3K Activated) |
|---|----------------------------------|----------------------------------|--------------------------------------|
| Total subjects affected by non-serious adverse events               |                                  |                                  |                                      |
| subjects affected / exposed   | 5 / 5 (100.00%)                  | 1 / 1 (100.00%)                  | 9 / 9 (100.00%)                      |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                  |                                  |                                      |
| Oncologic Complication  |                                  |                                  |                                      |
| subjects affected / exposed   | 0 / 5 (0.00%)                    | 0 / 1 (0.00%)                    | 0 / 9 (0.00%)                        |
| occurrences (all)   | 0                                | 0                                | 0                                    |
| Tumour Pain   |                                  |                                  |                                      |
| subjects affected / exposed   | 0 / 5 (0.00%)                    | 0 / 1 (0.00%)                    | 0 / 9 (0.00%)                        |
| occurrences (all)   | 0                                | 0                                | 0                                    |
| Vascular disorders  |                                  |                                  |                                      |
| Haematoma   |                                  |                                  |                                      |
| subjects affected / exposed   | 0 / 5 (0.00%)                    | 0 / 1 (0.00%)                    | 0 / 9 (0.00%)                        |
| occurrences (all)   | 0                                | 0                                | 0                                    |
| Hot Flush   |                                  |                                  |                                      |
| subjects affected / exposed   | 0 / 5 (0.00%)                    | 0 / 1 (0.00%)                    | 0 / 9 (0.00%)                        |
| occurrences (all)   | 0                                | 0                                | 0                                    |
| Hypertension  |                                  |                                  |                                      |

|  |                |               |                |
|--|----------------|---------------|----------------|
| subjects affected / exposed                          | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                                    | 0              | 0             | 0              |
| Hypotension  |                |               |                |
| subjects affected / exposed                          | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                                    | 0              | 0             | 0              |
| Lymphoedema  |                |               |                |
| subjects affected / exposed                          | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                                    | 0              | 0             | 0              |
| Pallor   |                |               |                |
| subjects affected / exposed                          | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                                    | 0              | 0             | 1              |
| Phlebitis  |                |               |                |
| subjects affected / exposed                          | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                                    | 0              | 0             | 1              |
| General disorders and administration site conditions |                |               |                |
| Asthenia   |                |               |                |
| subjects affected / exposed                          | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 3 / 9 (33.33%) |
| occurrences (all)                                    | 0              | 0             | 5              |
| Catheter Site Bruise                                 |                |               |                |
| subjects affected / exposed                          | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                                    | 0              | 0             | 0              |
| Catheter Site Oedema                                 |                |               |                |
| subjects affected / exposed                          | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                                    | 0              | 0             | 0              |
| Catheter Site Pain                                   |                |               |                |
| subjects affected / exposed                          | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                                    | 0              | 0             | 0              |
| Chills   |                |               |                |
| subjects affected / exposed                          | 1 / 5 (20.00%) | 0 / 1 (0.00%) | 2 / 9 (22.22%) |
| occurrences (all)                                    | 1              | 0             | 2              |
| Fatigue  |                |               |                |
| subjects affected / exposed                          | 3 / 5 (60.00%) | 0 / 1 (0.00%) | 6 / 9 (66.67%) |
| occurrences (all)                                    | 4              | 0             | 13             |
| Gait Disturbance                                     |                |               |                |

|                             |                |               |                |
|-----------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)           | 0              | 0             | 1              |
| Influenza Like Illness      |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Infusion Site Extravasation |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Infusion Site Rash          |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Malaise                     |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Medical Device Complication |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Mucosal Dryness             |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Mucosal Inflammation        |                |               |                |
| subjects affected / exposed | 2 / 5 (40.00%) | 0 / 1 (0.00%) | 3 / 9 (33.33%) |
| occurrences (all)           | 6              | 0             | 4              |
| Non-Cardiac Chest Pain      |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Oedema                      |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Oedema Peripheral           |                |               |                |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)           | 1              | 0             | 3              |
| Pain                        |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Pyrexia                     |                |               |                |

|  |                     |                    |                     |
|--|---------------------|--------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)   | 1 / 5 (20.00%)<br>1 | 0 / 1 (0.00%)<br>0 | 1 / 9 (11.11%)<br>1 |
| Immune system disorders<br>Hypersensitivity<br>subjects affected / exposed<br>occurrences (all)                | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Reproductive system and breast disorders<br>Pelvic Pain<br>subjects affected / exposed<br>occurrences (all)    | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Vaginal Haemorrhage<br>subjects affected / exposed<br>occurrences (all)  | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 | 1 / 9 (11.11%)<br>1 |
| Vulvovaginal Discomfort<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 | 1 / 9 (11.11%)<br>1 |
| Respiratory, thoracic and mediastinal disorders<br>Catarrh<br>subjects affected / exposed<br>occurrences (all) | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Cough<br>subjects affected / exposed<br>occurrences (all)  | 1 / 5 (20.00%)<br>1 | 0 / 1 (0.00%)<br>0 | 2 / 9 (22.22%)<br>2 |
| Dysphonia<br>subjects affected / exposed<br>occurrences (all)  | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)   | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 | 3 / 9 (33.33%)<br>3 |
| Dyspnoea Exertional<br>subjects affected / exposed<br>occurrences (all)  | 1 / 5 (20.00%)<br>1 | 0 / 1 (0.00%)<br>0 | 1 / 9 (11.11%)<br>1 |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)  | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Haemoptysis  |                     |                    |                     |



|                             |                |               |                |
|-----------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Oropharyngeal Pain          |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Pleural Effusion            |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Pneumonitis                 |                |               |                |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)           | 1              | 0             | 1              |
| Pneumothorax                |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Productive Cough            |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 2 / 9 (22.22%) |
| occurrences (all)           | 0              | 0             | 2              |
| Rhinalgia                   |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Upper-Airway Cough Syndrome |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Pleurisy                    |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Psychiatric disorders       |                |               |                |
| Anxiety                     |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Bradyphrenia                |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Confusional State           |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)           | 0              | 0             | 1              |

|                                      |                |               |                |
|--------------------------------------|----------------|---------------|----------------|
| Delirium                             |                |               |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                    | 0              | 0             | 1              |
| Depression                           |                |               |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Dysthymic Disorder                   |                |               |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Hallucination                        |                |               |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Hallucination, Visual                |                |               |                |
| subjects affected / exposed          | 1 / 5 (20.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 1              | 0             | 0              |
| Insomnia                             |                |               |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Irritability                         |                |               |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Restlessness                         |                |               |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Investigations                       |                |               |                |
| Alanine Aminotransferase Increased   |                |               |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Aspartate Aminotransferase Increased |                |               |                |
| subjects affected / exposed          | 1 / 5 (20.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 1              | 0             | 0              |
| Blood Alkaline Phosphatase           |                |               |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Blood Alkaline Phosphatase Increased |                |               |                |

|                                       |                |               |                |
|---------------------------------------|----------------|---------------|----------------|
| subjects affected / exposed           | 1 / 5 (20.00%) | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                     | 1              | 0             | 1              |
| Blood Cholesterol Increased           |                |               |                |
| subjects affected / exposed           | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                     | 0              | 0             | 0              |
| Blood Creatinine                      |                |               |                |
| subjects affected / exposed           | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                     | 0              | 0             | 1              |
| Blood Lactate Dehydrogenase Increased |                |               |                |
| subjects affected / exposed           | 1 / 5 (20.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                     | 1              | 0             | 0              |
| Blood Magnesium Decreased             |                |               |                |
| subjects affected / exposed           | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                     | 0              | 0             | 0              |
| Blood Pressure Diastolic Increased    |                |               |                |
| subjects affected / exposed           | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                     | 0              | 0             | 0              |
| Blood Triglycerides Increased         |                |               |                |
| subjects affected / exposed           | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                     | 0              | 0             | 0              |
| Chest X-Ray Abnormal                  |                |               |                |
| subjects affected / exposed           | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                     | 0              | 0             | 0              |
| Electrocardiogram Qt Prolonged        |                |               |                |
| subjects affected / exposed           | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 2 / 9 (22.22%) |
| occurrences (all)                     | 0              | 0             | 3              |
| Glycosylated Haemoglobin Increased    |                |               |                |
| subjects affected / exposed           | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                     | 0              | 0             | 0              |
| Haemoglobin                           |                |               |                |
| subjects affected / exposed           | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                     | 0              | 0             | 0              |
| Lymphocyte Count Decreased            |                |               |                |
| subjects affected / exposed           | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                     | 0              | 0             | 0              |

|  |                     |                      |                     |
|--|---------------------|----------------------|---------------------|
| Neutrophil Count Decreased<br>subjects affected / exposed<br>occurrences (all)       | 0 / 5 (0.00%)<br>0  | 1 / 1 (100.00%)<br>2 | 0 / 9 (0.00%)<br>0  |
| Platelet Count Decreased<br>subjects affected / exposed<br>occurrences (all)         | 1 / 5 (20.00%)<br>1 | 1 / 1 (100.00%)<br>1 | 1 / 9 (11.11%)<br>1 |
| Weight Decreased<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 5 (20.00%)<br>1 | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| White Blood Cell Count Decreased<br>subjects affected / exposed<br>occurrences (all) | 0 / 5 (0.00%)<br>0  | 1 / 1 (100.00%)<br>1 | 0 / 9 (0.00%)<br>0  |
| Blood Creatinine Increased<br>subjects affected / exposed<br>occurrences (all)       | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 1 / 9 (11.11%)<br>1 |
| Injury, poisoning and procedural complications                                       |                     |                      |                     |
| Contusion<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| Fall<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| Fracture<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| Infusion Related Reaction<br>subjects affected / exposed<br>occurrences (all)        | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| Limb Injury<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| Pelvic Fracture<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| Vascular Access Complication   |                     |                      |                     |

|  |                    |                    |                    |
|--|--------------------|--------------------|--------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 5 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0 |
| Cardiac disorders                                |                    |                    |                    |
| Palpitations                                     |                    |                    |                    |
| subjects affected / exposed                      | 0 / 5 (0.00%)      | 0 / 1 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Sinus Tachycardia                                |                    |                    |                    |
| subjects affected / exposed                      | 0 / 5 (0.00%)      | 0 / 1 (0.00%)      | 1 / 9 (11.11%)     |
| occurrences (all)                                | 0                  | 0                  | 1                  |
| Nervous system disorders                         |                    |                    |                    |
| Ageusia  |                    |                    |                    |
| subjects affected / exposed                      | 0 / 5 (0.00%)      | 0 / 1 (0.00%)      | 1 / 9 (11.11%)     |
| occurrences (all)                                | 0                  | 0                  | 1                  |
| Amnesia  |                    |                    |                    |
| subjects affected / exposed                      | 0 / 5 (0.00%)      | 0 / 1 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Dizziness  |                    |                    |                    |
| subjects affected / exposed                      | 1 / 5 (20.00%)     | 0 / 1 (0.00%)      | 1 / 9 (11.11%)     |
| occurrences (all)                                | 1                  | 0                  | 1                  |
| Dysgeusia  |                    |                    |                    |
| subjects affected / exposed                      | 2 / 5 (40.00%)     | 0 / 1 (0.00%)      | 1 / 9 (11.11%)     |
| occurrences (all)                                | 2                  | 0                  | 1                  |
| Headache   |                    |                    |                    |
| subjects affected / exposed                      | 0 / 5 (0.00%)      | 0 / 1 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Hypersomnia                                      |                    |                    |                    |
| subjects affected / exposed                      | 0 / 5 (0.00%)      | 0 / 1 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Sciatica   |                    |                    |                    |
| subjects affected / exposed                      | 0 / 5 (0.00%)      | 0 / 1 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Somnolence                                       |                    |                    |                    |
| subjects affected / exposed                      | 0 / 5 (0.00%)      | 0 / 1 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Syncope  |                    |                    |                    |

|  |                     |                    |                    |
|--|---------------------|--------------------|--------------------|
| subjects affected / exposed<br>occurrences (all) | 1 / 5 (20.00%)<br>1 | 0 / 1 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0 |
| Blood and lymphatic system disorders             |                     |                    |                    |
| Anaemia  |                     |                    |                    |
| subjects affected / exposed                      | 0 / 5 (0.00%)       | 1 / 1 (100.00%)    | 1 / 9 (11.11%)     |
| occurrences (all)                                | 0                   | 1                  | 2                  |
| Leukopenia                                       |                     |                    |                    |
| subjects affected / exposed                      | 0 / 5 (0.00%)       | 0 / 1 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                   | 0                  | 0                  |
| Lymphadenopathy                                  |                     |                    |                    |
| subjects affected / exposed                      | 0 / 5 (0.00%)       | 0 / 1 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                   | 0                  | 0                  |
| Lymphopenia                                      |                     |                    |                    |
| subjects affected / exposed                      | 1 / 5 (20.00%)      | 0 / 1 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 2                   | 0                  | 0                  |
| Neutropenia                                      |                     |                    |                    |
| subjects affected / exposed                      | 0 / 5 (0.00%)       | 0 / 1 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                   | 0                  | 0                  |
| Ear and labyrinth disorders                      |                     |                    |                    |
| Ear Pain   |                     |                    |                    |
| subjects affected / exposed                      | 0 / 5 (0.00%)       | 0 / 1 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                   | 0                  | 0                  |
| External Ear Inflammation                        |                     |                    |                    |
| subjects affected / exposed                      | 0 / 5 (0.00%)       | 0 / 1 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                   | 0                  | 0                  |
| Vertigo  |                     |                    |                    |
| subjects affected / exposed                      | 0 / 5 (0.00%)       | 0 / 1 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                   | 0                  | 0                  |
| Eye disorders                                    |                     |                    |                    |
| Abnormal Sensation In Eye                        |                     |                    |                    |
| subjects affected / exposed                      | 0 / 5 (0.00%)       | 0 / 1 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                   | 0                  | 0                  |
| Eyelid Bleeding                                  |                     |                    |                    |
| subjects affected / exposed                      | 0 / 5 (0.00%)       | 0 / 1 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                   | 0                  | 0                  |
| Iritis   |                     |                    |                    |

|                             |                |               |               |
|-----------------------------|----------------|---------------|---------------|
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Vision Blurred              |                |               |               |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Visual Impairment           |                |               |               |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)           | 1              | 0             | 0             |
| Dry Eyes                    |                |               |               |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Gastrointestinal disorders  |                |               |               |
| Abdominal Discomfort        |                |               |               |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Abdominal Distension        |                |               |               |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)           | 1              | 0             | 0             |
| Abdominal Pain              |                |               |               |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)           | 1              | 0             | 0             |
| Abdominal Pain Lower        |                |               |               |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Abdominal Pain Upper        |                |               |               |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Aphthous Stomatitis         |                |               |               |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Ascites                     |                |               |               |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)           | 1              | 0             | 0             |
| Cheilitis                   |                |               |               |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |

|                                  |                |                 |                |
|----------------------------------|----------------|-----------------|----------------|
| Constipation                     |                |                 |                |
| subjects affected / exposed      | 1 / 5 (20.00%) | 0 / 1 (0.00%)   | 3 / 9 (33.33%) |
| occurrences (all)                | 1              | 0               | 3              |
| Diarrhoea                        |                |                 |                |
| subjects affected / exposed      | 4 / 5 (80.00%) | 0 / 1 (0.00%)   | 7 / 9 (77.78%) |
| occurrences (all)                | 5              | 0               | 18             |
| Dry Mouth                        |                |                 |                |
| subjects affected / exposed      | 1 / 5 (20.00%) | 1 / 1 (100.00%) | 2 / 9 (22.22%) |
| occurrences (all)                | 1              | 1               | 2              |
| Dyspepsia                        |                |                 |                |
| subjects affected / exposed      | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 2 / 9 (22.22%) |
| occurrences (all)                | 0              | 0               | 2              |
| Dysphagia                        |                |                 |                |
| subjects affected / exposed      | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)                | 0              | 0               | 0              |
| Gastritis                        |                |                 |                |
| subjects affected / exposed      | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)                | 0              | 0               | 0              |
| Gastrooesophageal Reflux Disease |                |                 |                |
| subjects affected / exposed      | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 1 / 9 (11.11%) |
| occurrences (all)                | 0              | 0               | 1              |
| Glossodynia                      |                |                 |                |
| subjects affected / exposed      | 1 / 5 (20.00%) | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)                | 1              | 0               | 0              |
| Haemorrhoids                     |                |                 |                |
| subjects affected / exposed      | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 1 / 9 (11.11%) |
| occurrences (all)                | 0              | 0               | 1              |
| Hyperchlorhydria                 |                |                 |                |
| subjects affected / exposed      | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)                | 0              | 0               | 0              |
| Hypoaesthesia Oral               |                |                 |                |
| subjects affected / exposed      | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)                | 0              | 0               | 0              |
| Lip Ulceration                   |                |                 |                |
| subjects affected / exposed      | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)                | 0              | 0               | 0              |



|                             |                |                 |                |
|-----------------------------|----------------|-----------------|----------------|
| Mouth Ulceration            |                |                 |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Nausea                      |                |                 |                |
| subjects affected / exposed | 3 / 5 (60.00%) | 1 / 1 (100.00%) | 5 / 9 (55.56%) |
| occurrences (all)           | 8              | 1               | 7              |
| Odynophagia                 |                |                 |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Oral Discomfort             |                |                 |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Oral Dysaesthesia           |                |                 |                |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 1              | 0               | 0              |
| Oral Pain                   |                |                 |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Proctalgia                  |                |                 |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Rectal Haemorrhage          |                |                 |                |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 1              | 0               | 0              |
| Stomatitis                  |                |                 |                |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 1 (0.00%)   | 4 / 9 (44.44%) |
| occurrences (all)           | 1              | 0               | 6              |
| Tooth Disorder              |                |                 |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Vomiting                    |                |                 |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 1 / 9 (11.11%) |
| occurrences (all)           | 0              | 0               | 3              |
| Noninfective Gingivitis     |                |                 |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |

|  |                |               |                |
|--|----------------|---------------|----------------|
| Hepatobiliary disorders                |                |               |                |
| Hepatotoxicity                         |                |               |                |
| subjects affected / exposed            | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Skin and subcutaneous tissue disorders |                |               |                |
| Alopecia                               |                |               |                |
| subjects affected / exposed            | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Dermatitis                             |                |               |                |
| subjects affected / exposed            | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                      | 0              | 0             | 3              |
| Dermatitis Contact                     |                |               |                |
| subjects affected / exposed            | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Dry Skin                               |                |               |                |
| subjects affected / exposed            | 2 / 5 (40.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 2              | 0             | 0              |
| Eczema                                 |                |               |                |
| subjects affected / exposed            | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Erythema                               |                |               |                |
| subjects affected / exposed            | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Hangnail                               |                |               |                |
| subjects affected / exposed            | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Hyperhidrosis                          |                |               |                |
| subjects affected / exposed            | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 3 / 9 (33.33%) |
| occurrences (all)                      | 0              | 0             | 3              |
| Ingrowing Nail                         |                |               |                |
| subjects affected / exposed            | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Nail Disorder                          |                |               |                |
| subjects affected / exposed            | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Night Sweats                           |                |               |                |

|  |                |               |                |
|--|----------------|---------------|----------------|
| subjects affected / exposed                | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                          | 0              | 0             | 0              |
| Onycholysis                                |                |               |                |
| subjects affected / exposed                | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                          | 0              | 0             | 0              |
| Pain Of Skin                               |                |               |                |
| subjects affected / exposed                | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                          | 0              | 0             | 0              |
| Palmar-Plantar Erythrodysesthesia Syndrome |                |               |                |
| subjects affected / exposed                | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                          | 0              | 0             | 0              |
| Papule                                     |                |               |                |
| subjects affected / exposed                | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                          | 0              | 0             | 0              |
| Pruritus                                   |                |               |                |
| subjects affected / exposed                | 2 / 5 (40.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                          | 2              | 0             | 0              |
| Purpura                                    |                |               |                |
| subjects affected / exposed                | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                          | 0              | 0             | 0              |
| Rash                                       |                |               |                |
| subjects affected / exposed                | 2 / 5 (40.00%) | 0 / 1 (0.00%) | 2 / 9 (22.22%) |
| occurrences (all)                          | 4              | 0             | 4              |
| Rash Generalised                           |                |               |                |
| subjects affected / exposed                | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                          | 0              | 0             | 0              |
| Rash Maculo-Papular                        |                |               |                |
| subjects affected / exposed                | 1 / 5 (20.00%) | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                          | 1              | 0             | 1              |
| Rash Papular                               |                |               |                |
| subjects affected / exposed                | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                          | 0              | 0             | 0              |
| Skin Disorder                              |                |               |                |
| subjects affected / exposed                | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                          | 0              | 0             | 0              |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| Skin Exfoliation                                |                |                 |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Skin Lesion                                     |                |                 |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Swelling Face                                   |                |                 |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Urticaria                                       |                |                 |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 1 / 1 (100.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 1               | 0              |
| Renal and urinary disorders                     |                |                 |                |
| Haematuria                                      |                |                 |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Proteinuria                                     |                |                 |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Renal Colic                                     |                |                 |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Urinary Incontinence                            |                |                 |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Urinary Retention                               |                |                 |                |
| subjects affected / exposed                     | 1 / 5 (20.00%) | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)                               | 1              | 0               | 0              |
| Urinary Tract Obstruction                       |                |                 |                |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Musculoskeletal and connective tissue disorders |                |                 |                |
| Arthralgia                                      |                |                 |                |
| subjects affected / exposed                     | 1 / 5 (20.00%) | 0 / 1 (0.00%)   | 1 / 9 (11.11%) |
| occurrences (all)                               | 1              | 0               | 1              |
| Back Pain                                       |                |                 |                |

|                             |                |               |                |
|-----------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 2 / 9 (22.22%) |
| occurrences (all)           | 0              | 0             | 3              |
| Fistula                     |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Inguinal Mass               |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)           | 0              | 0             | 1              |
| Muscle Spasms               |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Musculoskeletal Chest Pain  |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Myalgia                     |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Osteopenia                  |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Pain In Extremity           |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Infections and infestations |                |               |                |
| Bacteriuria                 |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Candida Infection           |                |               |                |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 1              | 0             | 0              |
| Conjunctivitis              |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Cystitis                    |                |               |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |

|                                  |               |               |                |
|----------------------------------|---------------|---------------|----------------|
| Folliculitis                     |               |               |                |
| subjects affected / exposed      | 0 / 5 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Fungal Skin Infection            |               |               |                |
| subjects affected / exposed      | 0 / 5 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Gastroenteritis                  |               |               |                |
| subjects affected / exposed      | 0 / 5 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Genital Herpes Zoster            |               |               |                |
| subjects affected / exposed      | 0 / 5 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Gingivitis                       |               |               |                |
| subjects affected / exposed      | 0 / 5 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Nasopharyngitis                  |               |               |                |
| subjects affected / exposed      | 0 / 5 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Oral Candidiasis                 |               |               |                |
| subjects affected / exposed      | 0 / 5 (0.00%) | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                | 0             | 0             | 1              |
| Oral Fungal Infection            |               |               |                |
| subjects affected / exposed      | 0 / 5 (0.00%) | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                | 0             | 0             | 1              |
| Oral Herpes                      |               |               |                |
| subjects affected / exposed      | 0 / 5 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Paronychia                       |               |               |                |
| subjects affected / exposed      | 0 / 5 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Pharyngitis                      |               |               |                |
| subjects affected / exposed      | 0 / 5 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Pneumocystis Jirovecii Pneumonia |               |               |                |
| subjects affected / exposed      | 0 / 5 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |

|  |                     |                    |                     |
|--|---------------------|--------------------|---------------------|
| Respiratory Tract Infection<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Rhinitis<br>subjects affected / exposed<br>occurrences (all)   | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Skin Infection<br>subjects affected / exposed<br>occurrences (all)   | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Upper Respiratory Tract Infection<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Urinary Tract Infection<br>subjects affected / exposed<br>occurrences (all)                                  | 1 / 5 (20.00%)<br>1 | 0 / 1 (0.00%)<br>0 | 2 / 9 (22.22%)<br>2 |
| Vulvitis<br>subjects affected / exposed<br>occurrences (all)   | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Herpes Zoster<br>subjects affected / exposed<br>occurrences (all)  | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Tooth infection<br>subjects affected / exposed<br>occurrences (all)  | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Metabolism and nutrition disorders<br>Decreased Appetite<br>subjects affected / exposed<br>occurrences (all) | 2 / 5 (40.00%)<br>2 | 0 / 1 (0.00%)<br>0 | 6 / 9 (66.67%)<br>6 |
| Dehydration<br>subjects affected / exposed<br>occurrences (all)  | 1 / 5 (20.00%)<br>1 | 0 / 1 (0.00%)<br>0 | 2 / 9 (22.22%)<br>2 |
| Diabetes Mellitus<br>subjects affected / exposed<br>occurrences (all)  | 0 / 5 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Hypercholesterolaemia  |                     |                    |                     |

|                             |                 |                 |                |
|-----------------------------|-----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 5 (0.00%)   | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0              |
| Hyperglycaemia              |                 |                 |                |
| subjects affected / exposed | 5 / 5 (100.00%) | 0 / 1 (0.00%)   | 7 / 9 (77.78%) |
| occurrences (all)           | 5               | 0               | 26             |
| Hyperkalaemia               |                 |                 |                |
| subjects affected / exposed | 0 / 5 (0.00%)   | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0              |
| Hypertriglyceridaemia       |                 |                 |                |
| subjects affected / exposed | 0 / 5 (0.00%)   | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0              |
| Hypoalbuminaemia            |                 |                 |                |
| subjects affected / exposed | 1 / 5 (20.00%)  | 0 / 1 (0.00%)   | 1 / 9 (11.11%) |
| occurrences (all)           | 1               | 0               | 1              |
| Hypocalcaemia               |                 |                 |                |
| subjects affected / exposed | 0 / 5 (0.00%)   | 0 / 1 (0.00%)   | 1 / 9 (11.11%) |
| occurrences (all)           | 0               | 0               | 2              |
| Hypoglycaemia               |                 |                 |                |
| subjects affected / exposed | 0 / 5 (0.00%)   | 0 / 1 (0.00%)   | 1 / 9 (11.11%) |
| occurrences (all)           | 0               | 0               | 2              |
| Hypokalaemia                |                 |                 |                |
| subjects affected / exposed | 1 / 5 (20.00%)  | 1 / 1 (100.00%) | 4 / 9 (44.44%) |
| occurrences (all)           | 1               | 2               | 5              |
| Hypomagnesaemia             |                 |                 |                |
| subjects affected / exposed | 1 / 5 (20.00%)  | 0 / 1 (0.00%)   | 4 / 9 (44.44%) |
| occurrences (all)           | 1               | 0               | 5              |
| Hyponatraemia               |                 |                 |                |
| subjects affected / exposed | 2 / 5 (40.00%)  | 0 / 1 (0.00%)   | 1 / 9 (11.11%) |
| occurrences (all)           | 2               | 0               | 1              |
| Hypophosphataemia           |                 |                 |                |
| subjects affected / exposed | 0 / 5 (0.00%)   | 0 / 1 (0.00%)   | 1 / 9 (11.11%) |
| occurrences (all)           | 0               | 0               | 2              |
| Hyperlipidaemia             |                 |                 |                |
| subjects affected / exposed | 0 / 5 (0.00%)   | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0              |



| <b>Non-serious adverse events</b>                                      | PF-04691502 6 mg<br>(PI3K Activated) | PF-05212384 154<br>mg (PI3K Basal) | Lead-in-cohort (LIC)<br>PF-04691502 (4 mg) |
|--|--------------------------------------|------------------------------------|--|
| Total subjects affected by non-serious<br>adverse events               |                                      |                                    |  |
| subjects affected / exposed  | 3 / 3 (100.00%)                      | 21 / 21 (100.00%)                  | 3 / 3 (100.00%)                            |
| Neoplasms benign, malignant and<br>unspecified (incl cysts and polyps) |                                      |                                    |  |
| Oncologic Complication   |                                      |                                    |  |
| subjects affected / exposed  | 0 / 3 (0.00%)                        | 1 / 21 (4.76%)                     | 0 / 3 (0.00%)                              |
| occurrences (all)  | 0                                    | 1                                  | 0  |
| Tumour Pain  |                                      |                                    |  |
| subjects affected / exposed  | 0 / 3 (0.00%)                        | 0 / 21 (0.00%)                     | 0 / 3 (0.00%)                              |
| occurrences (all)  | 0                                    | 0                                  | 0  |
| Vascular disorders   |                                      |                                    |  |
| Haematoma  |                                      |                                    |  |
| subjects affected / exposed  | 0 / 3 (0.00%)                        | 1 / 21 (4.76%)                     | 0 / 3 (0.00%)                              |
| occurrences (all)  | 0                                    | 1                                  | 0  |
| Hot Flush  |                                      |                                    |  |
| subjects affected / exposed  | 0 / 3 (0.00%)                        | 0 / 21 (0.00%)                     | 0 / 3 (0.00%)                              |
| occurrences (all)  | 0                                    | 0                                  | 0  |
| Hypertension   |                                      |                                    |  |
| subjects affected / exposed  | 0 / 3 (0.00%)                        | 4 / 21 (19.05%)                    | 0 / 3 (0.00%)                              |
| occurrences (all)  | 0                                    | 10                                 | 0  |
| Hypotension  |                                      |                                    |  |
| subjects affected / exposed  | 0 / 3 (0.00%)                        | 0 / 21 (0.00%)                     | 0 / 3 (0.00%)                              |
| occurrences (all)  | 0                                    | 0                                  | 0  |
| Lymphoedema  |                                      |                                    |  |
| subjects affected / exposed  | 0 / 3 (0.00%)                        | 0 / 21 (0.00%)                     | 0 / 3 (0.00%)                              |
| occurrences (all)  | 0                                    | 0                                  | 0  |
| Pallor   |                                      |                                    |  |
| subjects affected / exposed  | 0 / 3 (0.00%)                        | 1 / 21 (4.76%)                     | 0 / 3 (0.00%)                              |
| occurrences (all)  | 0                                    | 2                                  | 0  |
| Phlebitis  |                                      |                                    |  |
| subjects affected / exposed  | 0 / 3 (0.00%)                        | 1 / 21 (4.76%)                     | 0 / 3 (0.00%)                              |
| occurrences (all)  | 0                                    | 1                                  | 0  |
| General disorders and administration<br>site conditions                |                                      |                                    |  |
| Asthenia   |                                      |                                    |  |

|                             |                |                 |                |
|-----------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%)  | 7 / 21 (33.33%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 10              | 0              |
| Catheter Site Bruise        |                |                 |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Catheter Site Oedema        |                |                 |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Catheter Site Pain          |                |                 |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Chills                      |                |                 |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 2 / 21 (9.52%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 2               | 0              |
| Fatigue                     |                |                 |                |
| subjects affected / exposed | 2 / 3 (66.67%) | 5 / 21 (23.81%) | 1 / 3 (33.33%) |
| occurrences (all)           | 3              | 5               | 1              |
| Gait Disturbance            |                |                 |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Influenza Like Illness      |                |                 |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 21 (4.76%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0              |
| Infusion Site Extravasation |                |                 |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Infusion Site Rash          |                |                 |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 21 (4.76%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0              |
| Malaise                     |                |                 |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 2 / 21 (9.52%)  | 2 / 3 (66.67%) |
| occurrences (all)           | 0              | 11              | 4              |
| Medical Device Complication |                |                 |                |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 1              | 0               | 0              |
| Mucosal Dryness             |                |                 |                |

|   |                |                  |                |
|---|----------------|------------------|----------------|
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 21 (0.00%)   | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0              | 0                | 0              |
| Mucosal Inflammation                            |                |                  |                |
| subjects affected / exposed                     | 1 / 3 (33.33%) | 12 / 21 (57.14%) | 0 / 3 (0.00%)  |
| occurrences (all)                               | 3              | 22               | 0              |
| Non-Cardiac Chest Pain                          |                |                  |                |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 1 / 21 (4.76%)   | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0              | 1                | 0              |
| Oedema  |                |                  |                |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 1 / 21 (4.76%)   | 1 / 3 (33.33%) |
| occurrences (all)                               | 0              | 1                | 1              |
| Oedema Peripheral                               |                |                  |                |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 2 / 21 (9.52%)   | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0              | 2                | 0              |
| Pain  |                |                  |                |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 21 (0.00%)   | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0              | 0                | 0              |
| Pyrexia   |                |                  |                |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 2 / 21 (9.52%)   | 1 / 3 (33.33%) |
| occurrences (all)                               | 0              | 2                | 1              |
| Immune system disorders                         |                |                  |                |
| Hypersensitivity                                |                |                  |                |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 1 / 21 (4.76%)   | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0              | 1                | 0              |
| Reproductive system and breast disorders        |                |                  |                |
| Pelvic Pain                                     |                |                  |                |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 1 / 21 (4.76%)   | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0              | 1                | 0              |
| Vaginal Haemorrhage                             |                |                  |                |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 3 / 21 (14.29%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0              | 3                | 0              |
| Vulvovaginal Discomfort                         |                |                  |                |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 21 (0.00%)   | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0              | 0                | 0              |
| Respiratory, thoracic and mediastinal disorders |                |                  |                |

|                             |                |                 |                |
|-----------------------------|----------------|-----------------|----------------|
| Catarrh                     |                |                 |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 21 (4.76%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0              |
| Cough                       |                |                 |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 7 / 21 (33.33%) | 1 / 3 (33.33%) |
| occurrences (all)           | 0              | 9               | 1              |
| Dysphonia                   |                |                 |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 2 / 21 (9.52%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 2               | 0              |
| Dyspnoea                    |                |                 |                |
| subjects affected / exposed | 1 / 3 (33.33%) | 3 / 21 (14.29%) | 1 / 3 (33.33%) |
| occurrences (all)           | 1              | 7               | 1              |
| Dyspnoea Exertional         |                |                 |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Epistaxis                   |                |                 |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 21 (4.76%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 18              | 0              |
| Haemoptysis                 |                |                 |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 2 / 21 (9.52%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 2               | 0              |
| Oropharyngeal Pain          |                |                 |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 2 / 21 (9.52%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 4               | 0              |
| Pleural Effusion            |                |                 |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Pneumonitis                 |                |                 |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Pneumothorax                |                |                 |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Productive Cough            |                |                 |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |

|                             |                |                |               |
|-----------------------------|----------------|----------------|---------------|
| Rhinalgia                   |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Upper-Airway Cough Syndrome |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Pleurisy                    |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Psychiatric disorders       |                |                |               |
| Anxiety                     |                |                |               |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)           | 1              | 0              | 0             |
| Bradyphrenia                |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 21 (4.76%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Confusional State           |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 2 / 21 (9.52%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 2              | 0             |
| Delirium                    |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Depression                  |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 2 / 21 (9.52%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 2              | 0             |
| Dysthymic Disorder          |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Hallucination               |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 21 (4.76%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Hallucination, Visual       |                |                |               |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Insomnia                    |                |                |               |

|                                       |               |                |               |
|---------------------------------------|---------------|----------------|---------------|
| subjects affected / exposed           | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                     | 0             | 0              | 0             |
| Irritability                          |               |                |               |
| subjects affected / exposed           | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%) |
| occurrences (all)                     | 0             | 1              | 0             |
| Restlessness                          |               |                |               |
| subjects affected / exposed           | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%) |
| occurrences (all)                     | 0             | 1              | 0             |
| Investigations                        |               |                |               |
| Alanine Aminotransferase Increased    |               |                |               |
| subjects affected / exposed           | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                     | 0             | 0              | 0             |
| Aspartate Aminotransferase Increased  |               |                |               |
| subjects affected / exposed           | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                     | 0             | 0              | 0             |
| Blood Alkaline Phosphatase            |               |                |               |
| subjects affected / exposed           | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                     | 0             | 0              | 0             |
| Blood Alkaline Phosphatase Increased  |               |                |               |
| subjects affected / exposed           | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                     | 0             | 0              | 0             |
| Blood Cholesterol Increased           |               |                |               |
| subjects affected / exposed           | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%) |
| occurrences (all)                     | 0             | 2              | 0             |
| Blood Creatinine                      |               |                |               |
| subjects affected / exposed           | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                     | 0             | 0              | 0             |
| Blood Lactate Dehydrogenase Increased |               |                |               |
| subjects affected / exposed           | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                     | 0             | 0              | 0             |
| Blood Magnesium Decreased             |               |                |               |
| subjects affected / exposed           | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                     | 0             | 0              | 0             |
| Blood Pressure Diastolic Increased    |               |                |               |

|                                    |                |                 |                |
|------------------------------------|----------------|-----------------|----------------|
| subjects affected / exposed        | 0 / 3 (0.00%)  | 1 / 21 (4.76%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0              | 1               | 0              |
| Blood Triglycerides Increased      |                |                 |                |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Chest X-Ray Abnormal               |                |                 |                |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Electrocardiogram Qt Prolonged     |                |                 |                |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Glycosylated Haemoglobin Increased |                |                 |                |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 1 / 21 (4.76%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0              | 1               | 0              |
| Haemoglobin                        |                |                 |                |
| subjects affected / exposed        | 1 / 3 (33.33%) | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 1              | 0               | 0              |
| Lymphocyte Count Decreased         |                |                 |                |
| subjects affected / exposed        | 1 / 3 (33.33%) | 0 / 21 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                  | 2              | 0               | 1              |
| Neutrophil Count Decreased         |                |                 |                |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 1 / 21 (4.76%)  | 1 / 3 (33.33%) |
| occurrences (all)                  | 0              | 1               | 1              |
| Platelet Count Decreased           |                |                 |                |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Weight Decreased                   |                |                 |                |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 3 / 21 (14.29%) | 2 / 3 (66.67%) |
| occurrences (all)                  | 0              | 4               | 3              |
| White Blood Cell Count Decreased   |                |                 |                |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 1 / 21 (4.76%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0              | 1               | 0              |
| Blood Creatinine Increased         |                |                 |                |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 2 / 21 (9.52%)  | 1 / 3 (33.33%) |
| occurrences (all)                  | 0              | 4               | 1              |
| Injury, poisoning and procedural   |                |                 |                |

|                              |               |                |                |
|------------------------------|---------------|----------------|----------------|
| complications                |               |                |                |
| Contusion                    |               |                |                |
| subjects affected / exposed  | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%)  |
| occurrences (all)            | 0             | 1              | 0              |
| Fall                         |               |                |                |
| subjects affected / exposed  | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%)  |
| occurrences (all)            | 0             | 1              | 0              |
| Fracture                     |               |                |                |
| subjects affected / exposed  | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)            | 0             | 0              | 0              |
| Infusion Related Reaction    |               |                |                |
| subjects affected / exposed  | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)            | 0             | 0              | 0              |
| Limb Injury                  |               |                |                |
| subjects affected / exposed  | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)            | 0             | 0              | 0              |
| Pelvic Fracture              |               |                |                |
| subjects affected / exposed  | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%)  |
| occurrences (all)            | 0             | 1              | 0              |
| Vascular Access Complication |               |                |                |
| subjects affected / exposed  | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)            | 0             | 0              | 0              |
| Cardiac disorders            |               |                |                |
| Palpitations                 |               |                |                |
| subjects affected / exposed  | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all)            | 0             | 0              | 1              |
| Sinus Tachycardia            |               |                |                |
| subjects affected / exposed  | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)            | 0             | 0              | 0              |
| Nervous system disorders     |               |                |                |
| Ageusia                      |               |                |                |
| subjects affected / exposed  | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)            | 0             | 0              | 0              |
| Amnesia                      |               |                |                |
| subjects affected / exposed  | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)            | 0             | 0              | 0              |
| Dizziness                    |               |                |                |



|                                      |                |                 |               |
|--------------------------------------|----------------|-----------------|---------------|
| subjects affected / exposed          | 0 / 3 (0.00%)  | 3 / 21 (14.29%) | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 3               | 0             |
| Dysgeusia                            |                |                 |               |
| subjects affected / exposed          | 1 / 3 (33.33%) | 6 / 21 (28.57%) | 0 / 3 (0.00%) |
| occurrences (all)                    | 1              | 7               | 0             |
| Headache                             |                |                 |               |
| subjects affected / exposed          | 1 / 3 (33.33%) | 1 / 21 (4.76%)  | 0 / 3 (0.00%) |
| occurrences (all)                    | 1              | 1               | 0             |
| Hypersomnia                          |                |                 |               |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 1 / 21 (4.76%)  | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 1               | 0             |
| Sciatica                             |                |                 |               |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 0               | 0             |
| Somnolence                           |                |                 |               |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 1 / 21 (4.76%)  | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 1               | 0             |
| Syncope                              |                |                 |               |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 0               | 0             |
| Blood and lymphatic system disorders |                |                 |               |
| Anaemia                              |                |                 |               |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 2 / 21 (9.52%)  | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 2               | 0             |
| Leukopenia                           |                |                 |               |
| subjects affected / exposed          | 1 / 3 (33.33%) | 0 / 21 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                    | 1              | 0               | 0             |
| Lymphadenopathy                      |                |                 |               |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 1 / 21 (4.76%)  | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 1               | 0             |
| Lymphopenia                          |                |                 |               |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 0               | 0             |
| Neutropenia                          |                |                 |               |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 1 / 21 (4.76%)  | 0 / 3 (0.00%) |
| occurrences (all)                    | 0              | 4               | 0             |

|                             |               |                |                |
|-----------------------------|---------------|----------------|----------------|
| Ear and labyrinth disorders |               |                |                |
| Ear Pain                    |               |                |                |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 1              | 0              |
| External Ear Inflammation   |               |                |                |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Vertigo                     |               |                |                |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 21 (9.52%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 2              | 0              |
| Eye disorders               |               |                |                |
| Abnormal Sensation In Eye   |               |                |                |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Eyelid Bleeding             |               |                |                |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 1              | 0              |
| Iritis                      |               |                |                |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 1              | 0              |
| Vision Blurred              |               |                |                |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Visual Impairment           |               |                |                |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Dry Eyes                    |               |                |                |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 1              | 0              |
| Gastrointestinal disorders  |               |                |                |
| Abdominal Discomfort        |               |                |                |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all)           | 0             | 0              | 1              |
| Abdominal Distension        |               |                |                |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 1 / 3 (33.33%) |
| occurrences (all)           | 0             | 1              | 1              |
| Abdominal Pain              |               |                |                |

|                                  |                |                 |                |
|----------------------------------|----------------|-----------------|----------------|
| subjects affected / exposed      | 0 / 3 (0.00%)  | 3 / 21 (14.29%) | 0 / 3 (0.00%)  |
| occurrences (all)                | 0              | 3               | 0              |
| Abdominal Pain Lower             |                |                 |                |
| subjects affected / exposed      | 0 / 3 (0.00%)  | 2 / 21 (9.52%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 0              | 2               | 0              |
| Abdominal Pain Upper             |                |                 |                |
| subjects affected / exposed      | 0 / 3 (0.00%)  | 2 / 21 (9.52%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 0              | 4               | 0              |
| Aphthous Stomatitis              |                |                 |                |
| subjects affected / exposed      | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 0              | 0               | 0              |
| Ascites                          |                |                 |                |
| subjects affected / exposed      | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 0              | 0               | 0              |
| Cheilitis                        |                |                 |                |
| subjects affected / exposed      | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                | 0              | 0               | 1              |
| Constipation                     |                |                 |                |
| subjects affected / exposed      | 0 / 3 (0.00%)  | 7 / 21 (33.33%) | 1 / 3 (33.33%) |
| occurrences (all)                | 0              | 8               | 2              |
| Diarrhoea                        |                |                 |                |
| subjects affected / exposed      | 2 / 3 (66.67%) | 8 / 21 (38.10%) | 1 / 3 (33.33%) |
| occurrences (all)                | 3              | 10              | 2              |
| Dry Mouth                        |                |                 |                |
| subjects affected / exposed      | 2 / 3 (66.67%) | 3 / 21 (14.29%) | 0 / 3 (0.00%)  |
| occurrences (all)                | 2              | 3               | 0              |
| Dyspepsia                        |                |                 |                |
| subjects affected / exposed      | 0 / 3 (0.00%)  | 2 / 21 (9.52%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 0              | 3               | 0              |
| Dysphagia                        |                |                 |                |
| subjects affected / exposed      | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 0              | 0               | 0              |
| Gastritis                        |                |                 |                |
| subjects affected / exposed      | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 0              | 0               | 0              |
| Gastrooesophageal Reflux Disease |                |                 |                |

|                             |                |                  |                |
|-----------------------------|----------------|------------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%)   | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0                | 0              |
| Glossodynia                 |                |                  |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%)   | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0                | 0              |
| Haemorrhoids                |                |                  |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%)   | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0                | 0              |
| Hyperchlorhydria            |                |                  |                |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 21 (0.00%)   | 0 / 3 (0.00%)  |
| occurrences (all)           | 1              | 0                | 0              |
| Hypoaesthesia Oral          |                |                  |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%)   | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0                | 0              |
| Lip Ulceration              |                |                  |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 21 (4.76%)   | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 1                | 0              |
| Mouth Ulceration            |                |                  |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 21 (4.76%)   | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 1                | 0              |
| Nausea                      |                |                  |                |
| subjects affected / exposed | 1 / 3 (33.33%) | 12 / 21 (57.14%) | 1 / 3 (33.33%) |
| occurrences (all)           | 1              | 19               | 1              |
| Odynophagia                 |                |                  |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 21 (4.76%)   | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 1                | 0              |
| Oral Discomfort             |                |                  |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%)   | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0                | 0              |
| Oral Dysaesthesia           |                |                  |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 21 (4.76%)   | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 2                | 0              |
| Oral Pain                   |                |                  |                |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%)   | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0                | 0              |
| Proctalgia                  |                |                  |                |

|  |                |                 |                |
|--|----------------|-----------------|----------------|
| subjects affected / exposed            | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                      | 0              | 0               | 1              |
| Rectal Haemorrhage                     |                |                 |                |
| subjects affected / exposed            | 0 / 3 (0.00%)  | 1 / 21 (4.76%)  | 0 / 3 (0.00%)  |
| occurrences (all)                      | 0              | 1               | 0              |
| Stomatitis                             |                |                 |                |
| subjects affected / exposed            | 0 / 3 (0.00%)  | 5 / 21 (23.81%) | 1 / 3 (33.33%) |
| occurrences (all)                      | 0              | 23              | 1              |
| Tooth Disorder                         |                |                 |                |
| subjects affected / exposed            | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0              |
| Vomiting                               |                |                 |                |
| subjects affected / exposed            | 1 / 3 (33.33%) | 7 / 21 (33.33%) | 1 / 3 (33.33%) |
| occurrences (all)                      | 1              | 12              | 1              |
| Noninfective Gingivitis                |                |                 |                |
| subjects affected / exposed            | 0 / 3 (0.00%)  | 1 / 21 (4.76%)  | 0 / 3 (0.00%)  |
| occurrences (all)                      | 0              | 1               | 0              |
| Hepatobiliary disorders                |                |                 |                |
| Hepatotoxicity                         |                |                 |                |
| subjects affected / exposed            | 0 / 3 (0.00%)  | 2 / 21 (9.52%)  | 0 / 3 (0.00%)  |
| occurrences (all)                      | 0              | 4               | 0              |
| Skin and subcutaneous tissue disorders |                |                 |                |
| Alopecia                               |                |                 |                |
| subjects affected / exposed            | 0 / 3 (0.00%)  | 3 / 21 (14.29%) | 0 / 3 (0.00%)  |
| occurrences (all)                      | 0              | 3               | 0              |
| Dermatitis                             |                |                 |                |
| subjects affected / exposed            | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0              |
| Dermatitis Contact                     |                |                 |                |
| subjects affected / exposed            | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                      | 0              | 0               | 1              |
| Dry Skin                               |                |                 |                |
| subjects affected / exposed            | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0              |
| Eczema                                 |                |                 |                |

|  |               |                |                |
|--|---------------|----------------|----------------|
| subjects affected / exposed                | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 1 / 3 (33.33%) |
| occurrences (all)                          | 0             | 1              | 1              |
| Erythema                                   |               |                |                |
| subjects affected / exposed                | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 1 / 3 (33.33%) |
| occurrences (all)                          | 0             | 1              | 1              |
| Hangnail                                   |               |                |                |
| subjects affected / exposed                | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%)  |
| occurrences (all)                          | 0             | 1              | 0              |
| Hyperhidrosis                              |               |                |                |
| subjects affected / exposed                | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%)  |
| occurrences (all)                          | 0             | 1              | 0              |
| Ingrowing Nail                             |               |                |                |
| subjects affected / exposed                | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                          | 0             | 0              | 0              |
| Nail Disorder                              |               |                |                |
| subjects affected / exposed                | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%)  |
| occurrences (all)                          | 0             | 1              | 0              |
| Night Sweats                               |               |                |                |
| subjects affected / exposed                | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%)  |
| occurrences (all)                          | 0             | 1              | 0              |
| Onycholysis                                |               |                |                |
| subjects affected / exposed                | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%)  |
| occurrences (all)                          | 0             | 1              | 0              |
| Pain Of Skin                               |               |                |                |
| subjects affected / exposed                | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                          | 0             | 0              | 0              |
| Palmar-Plantar Erythrodysesthesia Syndrome |               |                |                |
| subjects affected / exposed                | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%)  |
| occurrences (all)                          | 0             | 1              | 0              |
| Papule                                     |               |                |                |
| subjects affected / exposed                | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                          | 0             | 0              | 0              |
| Pruritus                                   |               |                |                |
| subjects affected / exposed                | 0 / 3 (0.00%) | 2 / 21 (9.52%) | 0 / 3 (0.00%)  |
| occurrences (all)                          | 0             | 2              | 0              |

|                             |                |                 |                 |
|-----------------------------|----------------|-----------------|-----------------|
| Purpura                     |                |                 |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)   |
| occurrences (all)           | 0              | 0               | 0               |
| Rash                        |                |                 |                 |
| subjects affected / exposed | 1 / 3 (33.33%) | 6 / 21 (28.57%) | 3 / 3 (100.00%) |
| occurrences (all)           | 1              | 9               | 6               |
| Rash Generalised            |                |                 |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 21 (4.76%)  | 0 / 3 (0.00%)   |
| occurrences (all)           | 0              | 3               | 0               |
| Rash Maculo-Papular         |                |                 |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 2 / 21 (9.52%)  | 0 / 3 (0.00%)   |
| occurrences (all)           | 0              | 3               | 0               |
| Rash Papular                |                |                 |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)   |
| occurrences (all)           | 0              | 0               | 0               |
| Skin Disorder               |                |                 |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)   |
| occurrences (all)           | 0              | 0               | 0               |
| Skin Exfoliation            |                |                 |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)   |
| occurrences (all)           | 0              | 0               | 0               |
| Skin Lesion                 |                |                 |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)   |
| occurrences (all)           | 0              | 0               | 0               |
| Swelling Face               |                |                 |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)   |
| occurrences (all)           | 0              | 0               | 0               |
| Urticaria                   |                |                 |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)   |
| occurrences (all)           | 0              | 0               | 0               |
| Renal and urinary disorders |                |                 |                 |
| Haematuria                  |                |                 |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)   |
| occurrences (all)           | 0              | 0               | 0               |
| Proteinuria                 |                |                 |                 |

|   |               |                |               |
|---|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 2              | 0             |
| Renal Colic                                     |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 2 / 21 (9.52%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 2              | 0             |
| Urinary Incontinence                            |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |
| Urinary Retention                               |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 1              | 0             |
| Urinary Tract Obstruction                       |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 2              | 0             |
| Musculoskeletal and connective tissue disorders |               |                |               |
| Arthralgia                                      |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 1              | 0             |
| Back Pain                                       |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 3              | 0             |
| Fistula   |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 1              | 0             |
| Inguinal Mass                                   |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |
| Muscle Spasms                                   |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 1              | 0             |
| Musculoskeletal Chest Pain                      |               |                |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 0             | 1              | 0             |
| Myalgia   |               |                |               |



|                             |               |                |                |
|-----------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 1              | 0              |
| Osteopenia                  |               |                |                |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 1              | 0              |
| Pain In Extremity           |               |                |                |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 1              | 0              |
| Infections and infestations |               |                |                |
| Bacteriuria                 |               |                |                |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Candida Infection           |               |                |                |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Conjunctivitis              |               |                |                |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 4              | 0              |
| Cystitis                    |               |                |                |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 1              | 0              |
| Folliculitis                |               |                |                |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all)           | 0             | 0              | 2              |
| Fungal Skin Infection       |               |                |                |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 1              | 0              |
| Gastroenteritis             |               |                |                |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 1              | 0              |
| Genital Herpes Zoster       |               |                |                |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Gingivitis                  |               |                |                |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 21 (9.52%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0             | 2              | 0              |

|                                   |               |                 |                |
|-----------------------------------|---------------|-----------------|----------------|
| Nasopharyngitis                   |               |                 |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 1 / 21 (4.76%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0             | 1               | 0              |
| Oral Candidiasis                  |               |                 |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0             | 0               | 0              |
| Oral Fungal Infection             |               |                 |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0             | 0               | 0              |
| Oral Herpes                       |               |                 |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0             | 0               | 0              |
| Paronychia                        |               |                 |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 1 / 21 (4.76%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0             | 2               | 0              |
| Pharyngitis                       |               |                 |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 1 / 21 (4.76%)  | 1 / 3 (33.33%) |
| occurrences (all)                 | 0             | 1               | 5              |
| Pneumocystis Jirovecii Pneumonia  |               |                 |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 21 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                 | 0             | 0               | 1              |
| Respiratory Tract Infection       |               |                 |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0             | 0               | 0              |
| Rhinitis                          |               |                 |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 3 / 21 (14.29%) | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0             | 3               | 0              |
| Skin Infection                    |               |                 |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 1 / 21 (4.76%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0             | 1               | 0              |
| Upper Respiratory Tract Infection |               |                 |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 21 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                 | 0             | 0               | 2              |
| Urinary Tract Infection           |               |                 |                |
| subjects affected / exposed       | 0 / 3 (0.00%) | 3 / 21 (14.29%) | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0             | 4               | 0              |

|                                    |                |                 |                |
|------------------------------------|----------------|-----------------|----------------|
| Vulvitis                           |                |                 |                |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Herpes Zoster                      |                |                 |                |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 1 / 21 (4.76%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0              | 2               | 0              |
| Tooth infection                    |                |                 |                |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 1 / 21 (4.76%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0              | 1               | 0              |
| Metabolism and nutrition disorders |                |                 |                |
| Decreased Appetite                 |                |                 |                |
| subjects affected / exposed        | 1 / 3 (33.33%) | 9 / 21 (42.86%) | 0 / 3 (0.00%)  |
| occurrences (all)                  | 1              | 21              | 0              |
| Dehydration                        |                |                 |                |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Diabetes Mellitus                  |                |                 |                |
| subjects affected / exposed        | 1 / 3 (33.33%) | 1 / 21 (4.76%)  | 1 / 3 (33.33%) |
| occurrences (all)                  | 2              | 1               | 1              |
| Hypercholesterolaemia              |                |                 |                |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 2 / 21 (9.52%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0              | 6               | 0              |
| Hyperglycaemia                     |                |                 |                |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 4 / 21 (19.05%) | 2 / 3 (66.67%) |
| occurrences (all)                  | 0              | 6               | 2              |
| Hyperkalaemia                      |                |                 |                |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 1 / 21 (4.76%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0              | 2               | 0              |
| Hypertriglyceridaemia              |                |                 |                |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 3 / 21 (14.29%) | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0              | 3               | 0              |
| Hypoalbuminaemia                   |                |                 |                |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 0 / 21 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Hypocalcaemia                      |                |                 |                |

|                             |               |                |               |
|-----------------------------|---------------|----------------|---------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Hypoglycaemia               |               |                |               |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Hypokalaemia                |               |                |               |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0             | 2              | 0             |
| Hypomagnesaemia             |               |                |               |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0             | 2              | 0             |
| Hyponatraemia               |               |                |               |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Hypophosphataemia           |               |                |               |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 21 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Hyperlipidaemia             |               |                |               |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 21 (4.76%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0             | 1              | 0             |

| <b>Non-serious adverse events</b>                                   | PF-05212384 154 mg (PI3K Activated) | LIC PF-05212384 (89 mg) | LIC PF-05212384 (154 mg) |
|---|-------------------------------------|-------------------------|--------------------------|
| Total subjects affected by non-serious adverse events               |                                     |                         |                          |
| subjects affected / exposed   | 18 / 19 (94.74%)                    | 3 / 3 (100.00%)         | 3 / 3 (100.00%)          |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                     |                         |                          |
| Oncologic Complication  |                                     |                         |                          |
| subjects affected / exposed   | 0 / 19 (0.00%)                      | 0 / 3 (0.00%)           | 0 / 3 (0.00%)            |
| occurrences (all)   | 0                                   | 0                       | 0                        |
| Tumour Pain   |                                     |                         |                          |
| subjects affected / exposed   | 0 / 19 (0.00%)                      | 1 / 3 (33.33%)          | 0 / 3 (0.00%)            |
| occurrences (all)   | 0                                   | 1                       | 0                        |
| Vascular disorders  |                                     |                         |                          |
| Haematoma   |                                     |                         |                          |
| subjects affected / exposed   | 0 / 19 (0.00%)                      | 0 / 3 (0.00%)           | 0 / 3 (0.00%)            |
| occurrences (all)   | 0                                   | 0                       | 0                        |
| Hot Flush   |                                     |                         |                          |

|  |                 |                |                |
|--|-----------------|----------------|----------------|
| subjects affected / exposed                          | 1 / 19 (5.26%)  | 1 / 3 (33.33%) | 0 / 3 (0.00%)  |
| occurrences (all)                                    | 1               | 1              | 0              |
| Hypertension   |                 |                |                |
| subjects affected / exposed                          | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                                    | 0               | 0              | 1              |
| Hypotension  |                 |                |                |
| subjects affected / exposed                          | 2 / 19 (10.53%) | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                                    | 2               | 0              | 0              |
| Lymphoedema  |                 |                |                |
| subjects affected / exposed                          | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                                    | 1               | 0              | 0              |
| Pallor   |                 |                |                |
| subjects affected / exposed                          | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                                    | 0               | 0              | 0              |
| Phlebitis  |                 |                |                |
| subjects affected / exposed                          | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                                    | 0               | 0              | 0              |
| General disorders and administration site conditions |                 |                |                |
| Asthenia   |                 |                |                |
| subjects affected / exposed                          | 2 / 19 (10.53%) | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                                    | 3               | 0              | 0              |
| Catheter Site Bruise                                 |                 |                |                |
| subjects affected / exposed                          | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                                    | 1               | 0              | 0              |
| Catheter Site Oedema                                 |                 |                |                |
| subjects affected / exposed                          | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                                    | 1               | 0              | 0              |
| Catheter Site Pain                                   |                 |                |                |
| subjects affected / exposed                          | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                                    | 1               | 0              | 0              |
| Chills   |                 |                |                |
| subjects affected / exposed                          | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                                    | 1               | 0              | 0              |
| Fatigue  |                 |                |                |

|                             |                  |                |                |
|-----------------------------|------------------|----------------|----------------|
| subjects affected / exposed | 10 / 19 (52.63%) | 0 / 3 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)           | 19               | 0              | 3              |
| Gait Disturbance            |                  |                |                |
| subjects affected / exposed | 0 / 19 (0.00%)   | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0                | 0              | 0              |
| Influenza Like Illness      |                  |                |                |
| subjects affected / exposed | 0 / 19 (0.00%)   | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0                | 0              | 0              |
| Infusion Site Extravasation |                  |                |                |
| subjects affected / exposed | 0 / 19 (0.00%)   | 1 / 3 (33.33%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0                | 1              | 0              |
| Infusion Site Rash          |                  |                |                |
| subjects affected / exposed | 0 / 19 (0.00%)   | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0                | 0              | 0              |
| Malaise                     |                  |                |                |
| subjects affected / exposed | 1 / 19 (5.26%)   | 1 / 3 (33.33%) | 2 / 3 (66.67%) |
| occurrences (all)           | 11               | 2              | 2              |
| Medical Device Complication |                  |                |                |
| subjects affected / exposed | 0 / 19 (0.00%)   | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0                | 0              | 0              |
| Mucosal Dryness             |                  |                |                |
| subjects affected / exposed | 1 / 19 (5.26%)   | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 1                | 0              | 0              |
| Mucosal Inflammation        |                  |                |                |
| subjects affected / exposed | 8 / 19 (42.11%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 17               | 0              | 0              |
| Non-Cardiac Chest Pain      |                  |                |                |
| subjects affected / exposed | 1 / 19 (5.26%)   | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 1                | 0              | 0              |
| Oedema                      |                  |                |                |
| subjects affected / exposed | 2 / 19 (10.53%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 2                | 0              | 0              |
| Oedema Peripheral           |                  |                |                |
| subjects affected / exposed | 5 / 19 (26.32%)  | 1 / 3 (33.33%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 7                | 1              | 0              |
| Pain                        |                  |                |                |

|   |                 |               |                |
|---|-----------------|---------------|----------------|
| subjects affected / exposed                     | 2 / 19 (10.53%) | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                               | 2               | 0             | 0              |
| Pyrexia   |                 |               |                |
| subjects affected / exposed                     | 2 / 19 (10.53%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all)                               | 2               | 0             | 1              |
| Immune system disorders                         |                 |               |                |
| Hypersensitivity                                |                 |               |                |
| subjects affected / exposed                     | 0 / 19 (0.00%)  | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0               | 0             | 0              |
| Reproductive system and breast disorders        |                 |               |                |
| Pelvic Pain                                     |                 |               |                |
| subjects affected / exposed                     | 0 / 19 (0.00%)  | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0               | 0             | 0              |
| Vaginal Haemorrhage                             |                 |               |                |
| subjects affected / exposed                     | 0 / 19 (0.00%)  | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0               | 0             | 0              |
| Vulvovaginal Discomfort                         |                 |               |                |
| subjects affected / exposed                     | 0 / 19 (0.00%)  | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0               | 0             | 0              |
| Respiratory, thoracic and mediastinal disorders |                 |               |                |
| Catarrh   |                 |               |                |
| subjects affected / exposed                     | 0 / 19 (0.00%)  | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0               | 0             | 0              |
| Cough   |                 |               |                |
| subjects affected / exposed                     | 3 / 19 (15.79%) | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                               | 3               | 0             | 0              |
| Dysphonia                                       |                 |               |                |
| subjects affected / exposed                     | 0 / 19 (0.00%)  | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0               | 0             | 0              |
| Dyspnoea  |                 |               |                |
| subjects affected / exposed                     | 3 / 19 (15.79%) | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                               | 4               | 0             | 0              |
| Dyspnoea Exertional                             |                 |               |                |
| subjects affected / exposed                     | 1 / 19 (5.26%)  | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                               | 1               | 0             | 0              |
| Epistaxis                                       |                 |               |                |

|                             |                 |                |                 |
|-----------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed | 2 / 19 (10.53%) | 1 / 3 (33.33%) | 0 / 3 (0.00%)   |
| occurrences (all)           | 4               | 2              | 0               |
| Haemoptysis                 |                 |                |                 |
| subjects affected / exposed | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)   |
| occurrences (all)           | 0               | 0              | 0               |
| Oropharyngeal Pain          |                 |                |                 |
| subjects affected / exposed | 3 / 19 (15.79%) | 0 / 3 (0.00%)  | 3 / 3 (100.00%) |
| occurrences (all)           | 3               | 0              | 5               |
| Pleural Effusion            |                 |                |                 |
| subjects affected / exposed | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)   |
| occurrences (all)           | 1               | 0              | 0               |
| Pneumonitis                 |                 |                |                 |
| subjects affected / exposed | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)   |
| occurrences (all)           | 0               | 0              | 0               |
| Pneumothorax                |                 |                |                 |
| subjects affected / exposed | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)   |
| occurrences (all)           | 1               | 0              | 0               |
| Productive Cough            |                 |                |                 |
| subjects affected / exposed | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)   |
| occurrences (all)           | 0               | 0              | 0               |
| Rhinalgia                   |                 |                |                 |
| subjects affected / exposed | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)   |
| occurrences (all)           | 1               | 0              | 0               |
| Upper-Airway Cough Syndrome |                 |                |                 |
| subjects affected / exposed | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)   |
| occurrences (all)           | 1               | 0              | 0               |
| Pleurisy                    |                 |                |                 |
| subjects affected / exposed | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)   |
| occurrences (all)           | 1               | 0              | 0               |
| Psychiatric disorders       |                 |                |                 |
| Anxiety                     |                 |                |                 |
| subjects affected / exposed | 2 / 19 (10.53%) | 0 / 3 (0.00%)  | 0 / 3 (0.00%)   |
| occurrences (all)           | 2               | 0              | 0               |
| Bradyphrenia                |                 |                |                 |
| subjects affected / exposed | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)   |
| occurrences (all)           | 0               | 0              | 0               |



|                                      |                 |                |                |
|--------------------------------------|-----------------|----------------|----------------|
| Confusional State                    |                 |                |                |
| subjects affected / exposed          | 2 / 19 (10.53%) | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 2               | 0              | 0              |
| Delirium                             |                 |                |                |
| subjects affected / exposed          | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| Depression                           |                 |                |                |
| subjects affected / exposed          | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 2               | 0              | 0              |
| Dysthymic Disorder                   |                 |                |                |
| subjects affected / exposed          | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 1               | 0              | 0              |
| Hallucination                        |                 |                |                |
| subjects affected / exposed          | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| Hallucination, Visual                |                 |                |                |
| subjects affected / exposed          | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| Insomnia                             |                 |                |                |
| subjects affected / exposed          | 3 / 19 (15.79%) | 1 / 3 (33.33%) | 0 / 3 (0.00%)  |
| occurrences (all)                    | 3               | 1              | 0              |
| Irritability                         |                 |                |                |
| subjects affected / exposed          | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| Restlessness                         |                 |                |                |
| subjects affected / exposed          | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| Investigations                       |                 |                |                |
| Alanine Aminotransferase Increased   |                 |                |                |
| subjects affected / exposed          | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                    | 1               | 0              | 3              |
| Aspartate Aminotransferase Increased |                 |                |                |
| subjects affected / exposed          | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                    | 1               | 0              | 2              |
| Blood Alkaline Phosphatase           |                 |                |                |

|                                       |                |               |                |
|---------------------------------------|----------------|---------------|----------------|
| subjects affected / exposed           | 1 / 19 (5.26%) | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                     | 2              | 0             | 0              |
| Blood Alkaline Phosphatase Increased  |                |               |                |
| subjects affected / exposed           | 1 / 19 (5.26%) | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                     | 1              | 0             | 0              |
| Blood Cholesterol Increased           |                |               |                |
| subjects affected / exposed           | 0 / 19 (0.00%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all)                     | 0              | 0             | 1              |
| Blood Creatinine                      |                |               |                |
| subjects affected / exposed           | 0 / 19 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                     | 0              | 0             | 0              |
| Blood Lactate Dehydrogenase Increased |                |               |                |
| subjects affected / exposed           | 1 / 19 (5.26%) | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                     | 1              | 0             | 0              |
| Blood Magnesium Decreased             |                |               |                |
| subjects affected / exposed           | 1 / 19 (5.26%) | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                     | 1              | 0             | 0              |
| Blood Pressure Diastolic Increased    |                |               |                |
| subjects affected / exposed           | 0 / 19 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                     | 0              | 0             | 0              |
| Blood Triglycerides Increased         |                |               |                |
| subjects affected / exposed           | 1 / 19 (5.26%) | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                     | 1              | 0             | 0              |
| Chest X-Ray Abnormal                  |                |               |                |
| subjects affected / exposed           | 1 / 19 (5.26%) | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                     | 1              | 0             | 0              |
| Electrocardiogram Qt Prolonged        |                |               |                |
| subjects affected / exposed           | 0 / 19 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                     | 0              | 0             | 0              |
| Glycosylated Haemoglobin Increased    |                |               |                |
| subjects affected / exposed           | 0 / 19 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)                     | 0              | 0             | 0              |
| Haemoglobin                           |                |               |                |

|  |                      |                     |                     |
|--|----------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                     | 0 / 19 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Lymphocyte Count Decreased<br>subjects affected / exposed<br>occurrences (all)       | 1 / 19 (5.26%)<br>4  | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Neutrophil Count Decreased<br>subjects affected / exposed<br>occurrences (all)       | 0 / 19 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Platelet Count Decreased<br>subjects affected / exposed<br>occurrences (all)         | 0 / 19 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Weight Decreased<br>subjects affected / exposed<br>occurrences (all)                 | 3 / 19 (15.79%)<br>9 | 1 / 3 (33.33%)<br>5 | 0 / 3 (0.00%)<br>0  |
| White Blood Cell Count Decreased<br>subjects affected / exposed<br>occurrences (all) | 0 / 19 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Blood Creatinine Increased<br>subjects affected / exposed<br>occurrences (all)       | 2 / 19 (10.53%)<br>2 | 0 / 3 (0.00%)<br>0  | 1 / 3 (33.33%)<br>1 |
| Injury, poisoning and procedural complications                                       |                      |                     |                     |
| Contusion<br>subjects affected / exposed<br>occurrences (all)                        | 1 / 19 (5.26%)<br>1  | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Fall<br>subjects affected / exposed<br>occurrences (all)                             | 1 / 19 (5.26%)<br>2  | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Fracture<br>subjects affected / exposed<br>occurrences (all)                         | 1 / 19 (5.26%)<br>2  | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Infusion Related Reaction<br>subjects affected / exposed<br>occurrences (all)        | 2 / 19 (10.53%)<br>2 | 0 / 3 (0.00%)<br>0  | 1 / 3 (33.33%)<br>1 |
| Limb Injury  |                      |                     |                     |

|                              |                 |                |                |
|------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed  | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)            | 1               | 0              | 0              |
| Pelvic Fracture              |                 |                |                |
| subjects affected / exposed  | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)            | 0               | 0              | 0              |
| Vascular Access Complication |                 |                |                |
| subjects affected / exposed  | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)            | 1               | 0              | 0              |
| Cardiac disorders            |                 |                |                |
| Palpitations                 |                 |                |                |
| subjects affected / exposed  | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)            | 0               | 0              | 0              |
| Sinus Tachycardia            |                 |                |                |
| subjects affected / exposed  | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)            | 0               | 0              | 0              |
| Nervous system disorders     |                 |                |                |
| Ageusia                      |                 |                |                |
| subjects affected / exposed  | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)            | 1               | 0              | 0              |
| Amnesia                      |                 |                |                |
| subjects affected / exposed  | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)            | 1               | 0              | 0              |
| Dizziness                    |                 |                |                |
| subjects affected / exposed  | 3 / 19 (15.79%) | 0 / 3 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)            | 3               | 0              | 1              |
| Dysgeusia                    |                 |                |                |
| subjects affected / exposed  | 8 / 19 (42.11%) | 0 / 3 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)            | 27              | 0              | 2              |
| Headache                     |                 |                |                |
| subjects affected / exposed  | 2 / 19 (10.53%) | 1 / 3 (33.33%) | 0 / 3 (0.00%)  |
| occurrences (all)            | 2               | 1              | 0              |
| Hypersomnia                  |                 |                |                |
| subjects affected / exposed  | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)            | 0               | 0              | 0              |
| Sciatica                     |                 |                |                |

|                                      |                 |                |                |
|--------------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed          | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 2               | 0              | 0              |
| Somnolence                           |                 |                |                |
| subjects affected / exposed          | 4 / 19 (21.05%) | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 4               | 0              | 0              |
| Syncope                              |                 |                |                |
| subjects affected / exposed          | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| Blood and lymphatic system disorders |                 |                |                |
| Anaemia                              |                 |                |                |
| subjects affected / exposed          | 2 / 19 (10.53%) | 0 / 3 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                    | 2               | 0              | 1              |
| Leukopenia                           |                 |                |                |
| subjects affected / exposed          | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| Lymphadenopathy                      |                 |                |                |
| subjects affected / exposed          | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| Lymphopenia                          |                 |                |                |
| subjects affected / exposed          | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| Neutropenia                          |                 |                |                |
| subjects affected / exposed          | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| Ear and labyrinth disorders          |                 |                |                |
| Ear Pain                             |                 |                |                |
| subjects affected / exposed          | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| External Ear Inflammation            |                 |                |                |
| subjects affected / exposed          | 0 / 19 (0.00%)  | 1 / 3 (33.33%) | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0               | 1              | 0              |
| Vertigo                              |                 |                |                |
| subjects affected / exposed          | 0 / 19 (0.00%)  | 1 / 3 (33.33%) | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0               | 1              | 0              |
| Eye disorders                        |                 |                |                |

|   |                      |                     |                     |
|---|----------------------|---------------------|---------------------|
| Abnormal Sensation In Eye<br>subjects affected / exposed<br>occurrences (all) | 1 / 19 (5.26%)<br>3  | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Eyelid Bleeding<br>subjects affected / exposed<br>occurrences (all)           | 0 / 19 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Iritis<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 19 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Vision Blurred<br>subjects affected / exposed<br>occurrences (all)            | 1 / 19 (5.26%)<br>1  | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Visual Impairment<br>subjects affected / exposed<br>occurrences (all)         | 0 / 19 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Dry Eyes<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 19 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 1 / 3 (33.33%)<br>0 |
| Gastrointestinal disorders  |                      |                     |                     |
| Abdominal Discomfort<br>subjects affected / exposed<br>occurrences (all)      | 0 / 19 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Abdominal Distension<br>subjects affected / exposed<br>occurrences (all)      | 0 / 19 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Abdominal Pain<br>subjects affected / exposed<br>occurrences (all)            | 4 / 19 (21.05%)<br>7 | 1 / 3 (33.33%)<br>1 | 1 / 3 (33.33%)<br>1 |
| Abdominal Pain Lower<br>subjects affected / exposed<br>occurrences (all)      | 1 / 19 (5.26%)<br>1  | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Abdominal Pain Upper<br>subjects affected / exposed<br>occurrences (all)      | 2 / 19 (10.53%)<br>2 | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Aphthous Stomatitis   |                      |                     |                     |

|                                  |                  |                |                |
|----------------------------------|------------------|----------------|----------------|
| subjects affected / exposed      | 1 / 19 (5.26%)   | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 1                | 0              | 0              |
| Ascites                          |                  |                |                |
| subjects affected / exposed      | 0 / 19 (0.00%)   | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 0                | 0              | 0              |
| Cheilitis                        |                  |                |                |
| subjects affected / exposed      | 0 / 19 (0.00%)   | 1 / 3 (33.33%) | 1 / 3 (33.33%) |
| occurrences (all)                | 0                | 1              | 1              |
| Constipation                     |                  |                |                |
| subjects affected / exposed      | 6 / 19 (31.58%)  | 0 / 3 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                | 7                | 0              | 1              |
| Diarrhoea                        |                  |                |                |
| subjects affected / exposed      | 10 / 19 (52.63%) | 1 / 3 (33.33%) | 0 / 3 (0.00%)  |
| occurrences (all)                | 24               | 1              | 0              |
| Dry Mouth                        |                  |                |                |
| subjects affected / exposed      | 4 / 19 (21.05%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 4                | 0              | 0              |
| Dyspepsia                        |                  |                |                |
| subjects affected / exposed      | 5 / 19 (26.32%)  | 1 / 3 (33.33%) | 0 / 3 (0.00%)  |
| occurrences (all)                | 9                | 1              | 0              |
| Dysphagia                        |                  |                |                |
| subjects affected / exposed      | 1 / 19 (5.26%)   | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 1                | 0              | 0              |
| Gastritis                        |                  |                |                |
| subjects affected / exposed      | 1 / 19 (5.26%)   | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 1                | 0              | 0              |
| Gastrooesophageal Reflux Disease |                  |                |                |
| subjects affected / exposed      | 1 / 19 (5.26%)   | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 1                | 0              | 0              |
| Glossodynia                      |                  |                |                |
| subjects affected / exposed      | 0 / 19 (0.00%)   | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 0                | 0              | 0              |
| Haemorrhoids                     |                  |                |                |
| subjects affected / exposed      | 0 / 19 (0.00%)   | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                | 0                | 0              | 0              |
| Hyperchlorhydria                 |                  |                |                |

|                             |                  |                 |                 |
|-----------------------------|------------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 19 (0.00%)   | 0 / 3 (0.00%)   | 0 / 3 (0.00%)   |
| occurrences (all)           | 0                | 0               | 0               |
| Hypoaesthesia Oral          |                  |                 |                 |
| subjects affected / exposed | 0 / 19 (0.00%)   | 0 / 3 (0.00%)   | 1 / 3 (33.33%)  |
| occurrences (all)           | 0                | 0               | 1               |
| Lip Ulceration              |                  |                 |                 |
| subjects affected / exposed | 0 / 19 (0.00%)   | 0 / 3 (0.00%)   | 0 / 3 (0.00%)   |
| occurrences (all)           | 0                | 0               | 0               |
| Mouth Ulceration            |                  |                 |                 |
| subjects affected / exposed | 1 / 19 (5.26%)   | 0 / 3 (0.00%)   | 0 / 3 (0.00%)   |
| occurrences (all)           | 1                | 0               | 0               |
| Nausea                      |                  |                 |                 |
| subjects affected / exposed | 10 / 19 (52.63%) | 3 / 3 (100.00%) | 3 / 3 (100.00%) |
| occurrences (all)           | 24               | 8               | 5               |
| Odynophagia                 |                  |                 |                 |
| subjects affected / exposed | 2 / 19 (10.53%)  | 0 / 3 (0.00%)   | 0 / 3 (0.00%)   |
| occurrences (all)           | 2                | 0               | 0               |
| Oral Discomfort             |                  |                 |                 |
| subjects affected / exposed | 1 / 19 (5.26%)   | 0 / 3 (0.00%)   | 0 / 3 (0.00%)   |
| occurrences (all)           | 1                | 0               | 0               |
| Oral Dysaesthesia           |                  |                 |                 |
| subjects affected / exposed | 0 / 19 (0.00%)   | 0 / 3 (0.00%)   | 0 / 3 (0.00%)   |
| occurrences (all)           | 0                | 0               | 0               |
| Oral Pain                   |                  |                 |                 |
| subjects affected / exposed | 1 / 19 (5.26%)   | 0 / 3 (0.00%)   | 0 / 3 (0.00%)   |
| occurrences (all)           | 1                | 0               | 0               |
| Proctalgia                  |                  |                 |                 |
| subjects affected / exposed | 2 / 19 (10.53%)  | 1 / 3 (33.33%)  | 0 / 3 (0.00%)   |
| occurrences (all)           | 2                | 1               | 0               |
| Rectal Haemorrhage          |                  |                 |                 |
| subjects affected / exposed | 0 / 19 (0.00%)   | 0 / 3 (0.00%)   | 0 / 3 (0.00%)   |
| occurrences (all)           | 0                | 0               | 0               |
| Stomatitis                  |                  |                 |                 |
| subjects affected / exposed | 3 / 19 (15.79%)  | 3 / 3 (100.00%) | 3 / 3 (100.00%) |
| occurrences (all)           | 16               | 12              | 7               |
| Tooth Disorder              |                  |                 |                 |



|  |                       |                     |                     |
|--|-----------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)   | 1 / 19 (5.26%)<br>1   | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)   | 7 / 19 (36.84%)<br>15 | 1 / 3 (33.33%)<br>1 | 1 / 3 (33.33%)<br>3 |
| Noninfective Gingivitis<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 19 (0.00%)<br>0   | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Hepatobiliary disorders<br>Hepatotoxicity<br>subjects affected / exposed<br>occurrences (all)          | 0 / 19 (0.00%)<br>0   | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Skin and subcutaneous tissue disorders<br>Alopecia<br>subjects affected / exposed<br>occurrences (all) | 1 / 19 (5.26%)<br>1   | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Dermatitis<br>subjects affected / exposed<br>occurrences (all)   | 0 / 19 (0.00%)<br>0   | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Dermatitis Contact<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 19 (0.00%)<br>0   | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Dry Skin<br>subjects affected / exposed<br>occurrences (all)   | 2 / 19 (10.53%)<br>3  | 1 / 3 (33.33%)<br>1 | 0 / 3 (0.00%)<br>0  |
| Eczema<br>subjects affected / exposed<br>occurrences (all)   | 0 / 19 (0.00%)<br>0   | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Erythema<br>subjects affected / exposed<br>occurrences (all)   | 0 / 19 (0.00%)<br>0   | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Hangnail<br>subjects affected / exposed<br>occurrences (all)   | 0 / 19 (0.00%)<br>0   | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  |
| Hyperhidrosis  |                       |                     |                     |

|   |                 |                |                |
|---|-----------------|----------------|----------------|
| subjects affected / exposed                 | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0               | 0              | 0              |
| Ingrowing Nail                              |                 |                |                |
| subjects affected / exposed                 | 0 / 19 (0.00%)  | 1 / 3 (33.33%) | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0               | 1              | 0              |
| Nail Disorder                               |                 |                |                |
| subjects affected / exposed                 | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0               | 0              | 0              |
| Night Sweats                                |                 |                |                |
| subjects affected / exposed                 | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0               | 0              | 0              |
| Onycholysis                                 |                 |                |                |
| subjects affected / exposed                 | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0               | 0              | 0              |
| Pain Of Skin                                |                 |                |                |
| subjects affected / exposed                 | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 1               | 0              | 0              |
| Palmar-Plantar Erythrodysaesthesia Syndrome |                 |                |                |
| subjects affected / exposed                 | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0               | 0              | 0              |
| Papule                                      |                 |                |                |
| subjects affected / exposed                 | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 3               | 0              | 0              |
| Pruritus                                    |                 |                |                |
| subjects affected / exposed                 | 2 / 19 (10.53%) | 1 / 3 (33.33%) | 2 / 3 (66.67%) |
| occurrences (all)                           | 9               | 5              | 2              |
| Purpura                                     |                 |                |                |
| subjects affected / exposed                 | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 1               | 0              | 0              |
| Rash  |                 |                |                |
| subjects affected / exposed                 | 3 / 19 (15.79%) | 1 / 3 (33.33%) | 2 / 3 (66.67%) |
| occurrences (all)                           | 4               | 17             | 2              |
| Rash Generalised                            |                 |                |                |
| subjects affected / exposed                 | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                           | 0               | 0              | 0              |

|                             |                 |                |                |
|-----------------------------|-----------------|----------------|----------------|
| Rash Maculo-Papular         |                 |                |                |
| subjects affected / exposed | 5 / 19 (26.32%) | 0 / 3 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)           | 9               | 0              | 3              |
| Rash Papular                |                 |                |                |
| subjects affected / exposed | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0              |
| Skin Disorder               |                 |                |                |
| subjects affected / exposed | 0 / 19 (0.00%)  | 1 / 3 (33.33%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0               | 1              | 0              |
| Skin Exfoliation            |                 |                |                |
| subjects affected / exposed | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0              |
| Skin Lesion                 |                 |                |                |
| subjects affected / exposed | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0              |
| Swelling Face               |                 |                |                |
| subjects affected / exposed | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0              |
| Urticaria                   |                 |                |                |
| subjects affected / exposed | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0              |
| Renal and urinary disorders |                 |                |                |
| Haematuria                  |                 |                |                |
| subjects affected / exposed | 3 / 19 (15.79%) | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 3               | 0              | 0              |
| Proteinuria                 |                 |                |                |
| subjects affected / exposed | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0              |
| Renal Colic                 |                 |                |                |
| subjects affected / exposed | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0              |
| Urinary Incontinence        |                 |                |                |
| subjects affected / exposed | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0              |
| Urinary Retention           |                 |                |                |

|   |                 |                |               |
|---|-----------------|----------------|---------------|
| subjects affected / exposed                     | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 1               | 0              | 0             |
| Urinary Tract Obstruction                       |                 |                |               |
| subjects affected / exposed                     | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0               | 0              | 0             |
| Musculoskeletal and connective tissue disorders |                 |                |               |
| Arthralgia                                      |                 |                |               |
| subjects affected / exposed                     | 4 / 19 (21.05%) | 0 / 3 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 12              | 0              | 0             |
| Back Pain                                       |                 |                |               |
| subjects affected / exposed                     | 3 / 19 (15.79%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all)                               | 3               | 1              | 0             |
| Fistula   |                 |                |               |
| subjects affected / exposed                     | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0               | 0              | 0             |
| Inguinal Mass                                   |                 |                |               |
| subjects affected / exposed                     | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0               | 0              | 0             |
| Muscle Spasms                                   |                 |                |               |
| subjects affected / exposed                     | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0               | 0              | 0             |
| Musculoskeletal Chest Pain                      |                 |                |               |
| subjects affected / exposed                     | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 1               | 0              | 0             |
| Myalgia   |                 |                |               |
| subjects affected / exposed                     | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 1               | 0              | 0             |
| Osteopenia                                      |                 |                |               |
| subjects affected / exposed                     | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0               | 0              | 0             |
| Pain In Extremity                               |                 |                |               |
| subjects affected / exposed                     | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                               | 0               | 0              | 0             |
| Infections and infestations                     |                 |                |               |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Bacteriuria                 |                |                |                |
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0              |
| Candida Infection           |                |                |                |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Conjunctivitis              |                |                |                |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 3 (33.33%) | 1 / 3 (33.33%) |
| occurrences (all)           | 0              | 1              | 1              |
| Cystitis                    |                |                |                |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Folliculitis                |                |                |                |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Fungal Skin Infection       |                |                |                |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Gastroenteritis             |                |                |                |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Genital Herpes Zoster       |                |                |                |
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0              |
| Gingivitis                  |                |                |                |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Nasopharyngitis             |                |                |                |
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0              |
| Oral Candidiasis            |                |                |                |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Oral Fungal Infection       |                |                |                |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |

|                                   |                 |                |                |
|-----------------------------------|-----------------|----------------|----------------|
| Oral Herpes                       |                 |                |                |
| subjects affected / exposed       | 3 / 19 (15.79%) | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 3               | 0              | 0              |
| Paronychia                        |                 |                |                |
| subjects affected / exposed       | 0 / 19 (0.00%)  | 1 / 3 (33.33%) | 1 / 3 (33.33%) |
| occurrences (all)                 | 0               | 4              | 3              |
| Pharyngitis                       |                 |                |                |
| subjects affected / exposed       | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 3               | 0              | 0              |
| Pneumocystis Jirovecii Pneumonia  |                 |                |                |
| subjects affected / exposed       | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0               | 0              | 0              |
| Respiratory Tract Infection       |                 |                |                |
| subjects affected / exposed       | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 1               | 0              | 0              |
| Rhinitis                          |                 |                |                |
| subjects affected / exposed       | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 1               | 0              | 0              |
| Skin Infection                    |                 |                |                |
| subjects affected / exposed       | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                 | 0               | 0              | 6              |
| Upper Respiratory Tract Infection |                 |                |                |
| subjects affected / exposed       | 2 / 19 (10.53%) | 1 / 3 (33.33%) | 0 / 3 (0.00%)  |
| occurrences (all)                 | 3               | 4              | 0              |
| Urinary Tract Infection           |                 |                |                |
| subjects affected / exposed       | 5 / 19 (26.32%) | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 8               | 0              | 0              |
| Vulvitis                          |                 |                |                |
| subjects affected / exposed       | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                 | 0               | 0              | 1              |
| Herpes Zoster                     |                 |                |                |
| subjects affected / exposed       | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0               | 0              | 0              |
| Tooth infection                   |                 |                |                |
| subjects affected / exposed       | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0               | 0              | 0              |

|                                    |                 |                |                |
|------------------------------------|-----------------|----------------|----------------|
| Metabolism and nutrition disorders |                 |                |                |
| Decreased Appetite                 |                 |                |                |
| subjects affected / exposed        | 8 / 19 (42.11%) | 1 / 3 (33.33%) | 2 / 3 (66.67%) |
| occurrences (all)                  | 8               | 1              | 3              |
| Dehydration                        |                 |                |                |
| subjects affected / exposed        | 2 / 19 (10.53%) | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 2               | 0              | 0              |
| Diabetes Mellitus                  |                 |                |                |
| subjects affected / exposed        | 2 / 19 (10.53%) | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 5               | 0              | 0              |
| Hypercholesterolaemia              |                 |                |                |
| subjects affected / exposed        | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 1               | 0              | 0              |
| Hyperglycaemia                     |                 |                |                |
| subjects affected / exposed        | 3 / 19 (15.79%) | 0 / 3 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                  | 3               | 0              | 1              |
| Hyperkalaemia                      |                 |                |                |
| subjects affected / exposed        | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 2               | 0              | 0              |
| Hypertriglyceridaemia              |                 |                |                |
| subjects affected / exposed        | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                  | 0               | 0              | 1              |
| Hypoalbuminaemia                   |                 |                |                |
| subjects affected / exposed        | 4 / 19 (21.05%) | 0 / 3 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                  | 4               | 0              | 4              |
| Hypocalcaemia                      |                 |                |                |
| subjects affected / exposed        | 1 / 19 (5.26%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 1               | 0              | 0              |
| Hypoglycaemia                      |                 |                |                |
| subjects affected / exposed        | 0 / 19 (0.00%)  | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0               | 0              | 0              |
| Hypokalaemia                       |                 |                |                |
| subjects affected / exposed        | 2 / 19 (10.53%) | 0 / 3 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                  | 3               | 0              | 1              |
| Hypomagnesaemia                    |                 |                |                |

|                             |                 |               |                |
|-----------------------------|-----------------|---------------|----------------|
| subjects affected / exposed | 3 / 19 (15.79%) | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 4               | 0             | 0              |
| Hyponatraemia               |                 |               |                |
| subjects affected / exposed | 2 / 19 (10.53%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all)           | 2               | 0             | 1              |
| Hypophosphataemia           |                 |               |                |
| subjects affected / exposed | 0 / 19 (0.00%)  | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0               | 0             | 0              |
| Hyperlipidaemia             |                 |               |                |
| subjects affected / exposed | 0 / 19 (0.00%)  | 0 / 3 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0               | 0             | 0              |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment   |
|-----------------|---|
| 25 October 2011 | Amendment 1 <ul style="list-style-type: none"><li>• Clarification of starting dose for PF-05212384.</li><li>• LIC, additional examinations and PK for Japanese patients.</li><li>• Clarification of eligibility criteria for Japanese patients.</li><li>• Lead-in PK sub-study.</li><li>• Addition of appendices relevant only to Japanese amendment.</li><li>• Other administrative changes.</li></ul>   |
| 17 April 2012   | Amendment 2<br>Clarification of starting dose for PF-05212384. <ul style="list-style-type: none"><li>• Addition of PK sub-study.</li><li>• Addition of PD endpoint of cholesterol and triglyceride changes.</li><li>• Updated safety text to match Company standards.</li><li>• Improvement of hyperglycemia management guidelines, including editing of two eligibility criteria.</li></ul>  |
| 03 August 2012  | Amendment 3 <ul style="list-style-type: none"><li>• Addition of additional PK blood draws in PK sub-study.</li><li>• Addition of language which defines end of survival follow-up period.</li><li>• Updated requirement for triglyceride and cholesterol testing (fasted state).</li><li>• Addition of standard Pfizer CSP template language regarding pregnancy testing for eligibility purposes and lifestyle guidelines with regards to birth control, safety data collection, temperature monitoring in drug storage area, and record retention.</li><li>• Clarification of language regarding statistical analysis of ECG data.</li><li>• Addition of language to clarify provision of study drug to patients in the event that the sponsor ended the study prematurely.</li></ul>   |
| 10 August 2012  | Amendment 4 (Japan Specific) <ul style="list-style-type: none"><li>• Addition of patients in LIC.</li><li>• Addition of PK blood draws in PK sub-study.</li><li>• Addition of PD endpoint of cholesterol and triglyceride changes (fasted state).</li><li>• Revision of hyperglycemia management guidelines, including editing of two eligibility criteria.</li><li>• Updated dose modification schedule for PF-04691502 and PF-05212384 in LIC.</li><li>• Updated safety text to match Company standards.</li><li>• Addition of language defining end of survival follow-up period.</li><li>• Addition of standard Pfizer CSP template language regarding pregnancy testing for eligibility purposes and lifestyle guidelines with regards to birth control, safety data collection, temperature monitoring in drug storage area, and record retention.</li><li>• Clarification of language regarding statistical analysis of ECG data.</li><li>• Updated guidelines for safety data reviewing.</li><li>• Addition of language to clarify provision of study drug to patients in the event that the sponsor ended the study prematurely.</li></ul> |
| 31 August 2012  | Amendment 5 <ul style="list-style-type: none"><li>• Reduction of the starting dose for PF-04691502.</li><li>• Reduction of the dose of PF-04691502 for ongoing patients.</li><li>• Updated phase 1 clinical data for PF-04691502 and PF-05212384.</li><li>• Addition of required CT scans of chest at baseline and every 8 weeks.</li><li>• Allowed for 20 patients with starting dose of 6 mg of PF-04691502 in Stage 1 for each PF-04691502 arm.</li><li>• Updated dose modification guidelines with respiratory toxicities.</li><li>• Modified CSP-specific SAEs.</li></ul>  |

|                   |  |
|-------------------|--|
| 10 September 2012 | <p>Amendment 6 (Japan Specific)</p> <ul style="list-style-type: none"> <li>• Reduction of the dose of PF-04691502 for ongoing patients of the main study.</li> <li>• Addition of 2 mg cohort in LIC.</li> <li>• Updated guidelines for safety data reviewing.</li> <li>• Updated phase 1 clinical data for PF-04691502 and PF-05212384.</li> <li>• Addition of required CT scans of chest at baseline and every 8 weeks.</li> <li>• Allowed for 20 patients with starting dose of 6 mg of PF-04691502 in Stage 1 for each PF-04691502 arm.</li> <li>• Updated dose modification guidelines with respiratory toxicities.</li> <li>• Modified CSP-specific SAEs.</li> </ul>  |
| 02 November 2012  | <p>Amendment 7</p> <ul style="list-style-type: none"> <li>• Enrollment to arms of the study which utilized PF-04691502 was discontinued.</li> <li>• Long term follow up portion of the study was removed for those patients on the PF-04691502 arms of the study.</li> <li>• Changed timing for pregnancy testing during screening.</li> <li>• Glucose testing changed to fasted or non-fasted for all study patients.</li> <li>• Post study SAE reporting requirements changed to specify that SAEs clearly related to subsequent anti-cancer treatments (including other clinical studies) or disease progression were not to be reported.</li> <li>• Patients on the PF-04691502 arms of the study no longer needed to perform blood draws for PK or optional tumor biopsies for PD.</li> <li>• There was no formal PK analysis for PF-04691502, only concentration-time listings.</li> <li>• Total number of patients enrolled to the study was changed as a result of stopping further enrollment to the PF-04691502 arms of the study.</li> <li>• Female patients of childbearing potential had to agree to use 2 methods of highly effective contraception.</li> <li>• Specific criteria for QTc analyses were removed, to be addressed in the SAP.</li> <li>• Removal of analysis of PF-04691502 concentration vs. QT.</li> </ul>  |
| 09 November 2012  | <p>Amendment 8 (Japan Specific) (09 November 2012)</p> <ul style="list-style-type: none"> <li>• Enrollment to arms of the study which utilized PF-04691502 was discontinued.</li> <li>• Long term follow up portion of the study was removed for those patients on the PF-04691502 arms of the study.</li> <li>• Changed timing for pregnancy testing during screening.</li> <li>• Glucose testing changed to fasted OR non-fasted for all study patients.</li> <li>• Post study SAE reporting requirements changed to specify that SAEs clearly related to subsequent anti-cancer treatments (including other clinical studies) or disease progression were not to be reported.</li> <li>• Patients on the PF-04691502 arms of the study no longer needed to perform blood draws for PK or optional tumor biopsies for PD.</li> <li>• There was no formal PK analysis for PF-04691502, only concentration-time listings.</li> <li>• Total number of patients enrolled to the study had changed as a result of stopping further enrollment to the PF-04691502 arms of the study.</li> <li>• Female subjects of childbearing potential had to agree to use 2 methods of highly effective contraception.</li> <li>• Specific criteria for QTc analyses were removed, to be addressed in the statistical analysis plan.</li> <li>• Removal of analysis of PF-04691502 concentration vs QT.</li> </ul> |
| 19 February 2015  | <p>Amendment 9 (Japan specific)</p> <ul style="list-style-type: none"> <li>• Text was added to describe termination of the study and rationale for termination.</li> <li>• Reduction of tumor assessment schedule.</li> <li>• Addition of plasma sampling for circulating DNA analysis.</li> <li>• Procedure for blood draw for this DNA analysis was added.</li> <li>• Study endpoint and objectives were updated accordingly to support this DNA analysis.</li> </ul>  |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date            | Interruption  | Restart date |
|-----------------|---|--------------|
| 23 January 2014 | Enrollment to B1271004 was discontinued on 23 January 2014 following a strategic decision based on initial results which were contrary to the hypothesis that a Stathmin high status (PI3K activated) would predict for better efficacy. The CSP indicated that the study would proceed into Stage 2 of the study if at least 8 clinical benefit responders were observed in 20 response evaluable patients at the end of Stage 1. As of 14 January 2014, 9 clinical benefit responders had been identified in the 'Stathmin low' arm of the study. Although this met the CSP defined criteria for advancement in to Stage 2 of the study, the sponsor determined not to proceed to Stage 2 based on the overall clinical findings. Patients who were already receiving treatment in Stage 1 of the study continued to take study drug. Patients were no longer followed up for OS and the planned OS analysis was not performed. | -            |

Notes:

## Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None

Notes: