



Clinical trial results:

A phase II study of pazopanib in patients with metastatic or unresectable renal cell carcinoma (RCC) who have failed prior sunitinib therapy

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2010-022770-13 |
| Trial protocol | IE SE |
| Global end of trial date | 15 July 2020 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 26 June 2022 |
| First version publication date | 26 June 2022 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | ICORG 10-01 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01566747 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Cancer Trials Ireland |
| Sponsor organisation address | Ardilaun House, St Stephens Green, Ireland, D02 VN51 |
| Public contact | Head of Clinical Operations, Cancer Trials Ireland, +353 16677211, regulatory@cancertrials.ie |
| Scientific contact | Head of Clinical Operations, Cancer Trials Ireland, +353 16677211, regulatory@cancertrials.ie |

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 | 01 July 2021 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 07 April 2020 |
| Global end of trial reached? | Yes |
| Global end of trial date | 15 July 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this trial is to assess the progression free rate at 4 months (i.e. completion of 4 months of treatment, with no disease progression at 8 weeks, and no evidence to suggest disease progression before the 4 month time-point).

Protection of trial subjects:

This clinical study was designed, implemented, and reported in accordance with the International Conference on Harmonization (ICH) Harmonized Tripartite Guidelines for Good Clinical Practice (GCP), with applicable local regulations SI 190 of 2004 as amend and European Directive 2001/20/EC. The study was approved by the HPRA and Cork Teaching Hospitals Clinical Research Ethics Committee on 12th Jan 2011.

Background therapy:

N/A all patients will receive Pazopanib. Patient must have also received prior treatment with sunitinib for at least 12 weeks in order to participate in this study. Prior treatment with either temsirolimus or everolimus will also be allowed as these treatments have been proven to be effective as 2nd line therapy of RCC.

Evidence for comparator:

The aim of this study is to assess the efficacy of pazopanib in treating patients with metastatic renal cell carcinoma whose cancer has progressed following treatment with sunitinib. As there are currently a number of small molecules approved in the RCC setting, major interest now lies in defining the best sequence of drugs and whether persistent targeting of the VEGF receptor family is warranted following failure of a prior VEGF directed therapy. Sunitinib is a multi-kinase inhibitor of VEGFR 1, VEGFR 2, VEGFR 3, PDGFR α/β , c kit, Flt-3, CSF-1 and RET while pazopanib is a selective inhibitor of VEGFR 1, 2, 3, PDGFR α/β and c kit. This study aims to assess if pazopanib retains activity against the RCC following progression on sunitinib therapy with the biological rationale being that the non-overlapping targets may confer different activity levels.

| | |
|---|---------------|
| Actual start date of recruitment | 08 March 2011 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Sweden: 3 |
| Country: Number of subjects enrolled | Ireland: 51 |
| Worldwide total number of subjects | 54 |
| EEA total number of subjects | 54 |

Notes:

Subjects enrolled per age group

| | |
|---|----|
| 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) | 36 |
| From 65 to 84 years | 18 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

54 patients were consented from 8 sites in Ireland and Sweden from 08-Mar-2011 until 05-Feb-2016

Pre-assignment

Screening details:

The target population for this study was patients with metastatic or unresectable renal cell carcinoma, who had been previously treated with sunitinib and relapsed. The patients had to meet all other inclusion criteria and none of the exclusion criteria.

Period 1

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

Blinding implementation details:

N/A As Blinding Not Used for Study.

Arms

| | |
|-----------|------------|
| Arm title | Single Arm |
|-----------|------------|

Arm description:

Phase II single arm study of pazopanib after failure of 1st Line therapy with sunitinib in patients with metastatic or unresectable RCC

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Pazopanib |
| Investigational medicinal product code | GW786034 |
| Other name | Votrient |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Pazopanib 800mg day to be given continuously until disease progression unacceptable toxicity or withdrawal of consent.

Pazopanib monohydrochloride is supplied as a series of aqueous film-coated tablets containing 200mg and 400mg of the freebase:

- 200mg, oval-shaped, white, packaged in bottles containing 34 tablets each
- 400mg, oval-shaped, white, packaged in bottles containing 68 tablets each

Starting on Day 1 of the Treatment Period, each subject will receive 800mg (2 X 400mg tablets) of pazopanib to be administered once daily by mouth. The 200mg tablets of pazopanib will be provided to subjects who need dose adjustments during the study

Response assessments were to be carried out every 8 weeks for the first 24 weeks (six months) and then every twelve weeks until disease progression. Safety assessments were to be carried out every 4 weeks for the first six months and then every eight weeks until disease progression.

| | |
|---------------------------------------|------------|
| Number of subjects in period 1 | Single Arm |
| Started | 54 |
| Completed | 4 |
| Not completed | 50 |
| Adverse event, serious fatal | 47 |
| Consent withdrawn by subject | 1 |

| | |
|-------------------|---|
| Study Closure | 1 |
| Lost to follow-up | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | Single Arm |
|-----------------------|------------|

Reporting group description: -

| Reporting group values | Single Arm | Total | |
|--|---------------|-------|--|
| Number of subjects | 54 | 54 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 18 | 18 | |
| From 65-84 years | 36 | 36 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| median | 58.5 | | |
| full range (min-max) | 40 to 81 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 13 | 13 | |
| Male | 41 | 41 | |
| Race | | | |
| Units: Subjects | | | |
| Caucasian | 54 | 54 | |
| Height at creening (cm) | | | |
| Units: cm | | | |
| median | 174 | | |
| full range (min-max) | 148 to 194 | - | |
| Weight at Screening | | | |
| Units: kg | | | |
| median | 79.8 | | |
| full range (min-max) | 46.6 to 138.2 | - | |

Subject analysis sets

| | |
|----------------------------|--------------|
| Subject analysis set title | Analysis Arm |
|----------------------------|--------------|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

As this is a single arm study, an extra arm is required to be added so that the statistical analysis can be added. This is NOT extra information or an extra arm. There is only one arm for this study. There were only 54 subjects analysed in total

| Reporting group values | Analysis Arm | | |
|---|--------------|--|--|
| Number of subjects | 54 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 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) | 18 | | |
| From 65-84 years | 36 | | |
| 85 years and over | 0 | | |
| Age continuous | | | |
| Units: years | | | |
| median | | | |
| full range (min-max) | | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | | | |
| Male | | | |
| Race | | | |
| Units: Subjects | | | |
| Caucasian | | | |
| Height at creening (cm) | | | |
| Units: cm | | | |
| median | | | |
| full range (min-max) | | | |
| Weight at Screening | | | |
| Units: kg | | | |
| median | | | |
| full range (min-max) | | | |

End points

End points reporting groups

| | |
|--|---------------|
| Reporting group title | Single Arm |
| Reporting group description: Phase II single arm study of pazopanib after failure of 1st Line therapy with sunitinib in patients with metastatic or unresectable RCC | |
| Subject analysis set title | Analysis Arm |
| Subject analysis set type | Full analysis |
| Subject analysis set description: As this is a single arm study, an extra arm is required to be added so that the statistical analysis can be added. This is NOT extra information or an extra arm. There is only one arm for this study. There were only 54 subjects analysed in total | |

Primary: Progression Free Rate at 4 Months

| | |
|---|-----------------------------------|
| End point title | Progression Free Rate at 4 Months |
| End point description: Progression Free-Rate at 4 months (i.e. completion of 4 months of treatment, with no disease progression at 8 weeks, and no evidence to suggest progression before the 4-month time-point). The PFS Rate was 23 Patients of 46 evaluable patients (50%) with a 95% CI. Simon's two-stage design required 25 of a planned 43 evaluable patients (50%) with a 95% CI. Simon's two-stage design requires 25 of a planned 43 evaluable patients to be progression free at 4-months in order to reject a PFS rate of 45%, so this unacceptable rate cannot be rejected. Progression Free = Complete Response (0 Patients) + Partial Response (7 Patients) + Stable Disease (16 Patients). As a check on robustness, the analysis was repeated for the Safety Set (all available data for the primary endpoint). The PFS rate was 24 patients of 48 patients (50.0%), with a 95% CI of [36.4 – 63.6]. This PFS rate also means that an unacceptable rate of 45% cannot be rejected. | |
| End point type | Primary |
| End point timeframe: From Time of Treatment Start Until 4 Months After Treatment start | |

| End point values | Single Arm | Analysis Arm | | |
|-----------------------------------|-------------------|----------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 46 | 46 ^[1] | | |
| Units: Patients | | | | |
| number (confidence interval 95%) | | | | |
| Progression Free Rate at 4 Months | 50 (36.1 to 63.9) | 50 (36.1 to 63.9) | | |

Notes:

[1] - The statistical arm is being used as it is a single arm study. Only 46 subjects were analysed total

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Progression-free survival rate at 4 months |
| Statistical analysis description: Progression-free survival rate | |
| Comparison groups | Single Arm v Analysis Arm |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 92 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[2] |
| Method | PFS Rate & CI |
| Parameter estimate | Progression-free survival rate |
| Point estimate | 50 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 36.1 |
| upper limit | 63.9 |

Notes:

[2] - Progression-free survival rate and confidence interval

Secondary: Median Time to Progression Free Survival (PFS)

| | |
|--|--|
| End point title | Median Time to Progression Free Survival (PFS) |
| End point description: | |
| Progression-free survival, defined as the length of time between the date of starting treatment and the earliest date of disease progression or death due to any cause. A total of 43 Patients (out of 48 - 89.6%) progressed on study treatment including 3 patients who discontinued study treatment for reason of clinical progression. | |
| End point type | Secondary |
| End point timeframe: | |
| Date of Starting Treatment and earliest date of disease progression or death due to any cause | |

| End point values | Single Arm | | | |
|----------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 48 | | | |
| Units: Months | | | | |
| number (confidence interval 95%) | | | | |
| Median Time to Progression | 4.76 (3.68 to 5.78) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall response rate (ORR)

| | |
|---|-----------------------------|
| End point title | Overall response rate (ORR) |
| End point description: | |
| Overall response rate (ORR), defined as the percentage of patients who achieved at least a partial response. It is Patients who had complete response + Partial Response. | |
| End point type | Secondary |
| End point timeframe: | |
| From start of study treatment until partial/complete response | |

| End point values | Single Arm | | | |
|--------------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 48 | | | |
| Units: Patients | | | | |
| number (confidence interval 95%) | | | | |
| Best Response During Study Treatment | 22.9 (13.3 to 36.5) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

| | |
|-----------------|------------------|
| End point title | Overall Survival |
|-----------------|------------------|

End point description:

Overall survival, defined as the length of time between the date of starting treatment and the date of death due to any cause. A total of 47 deaths (87.0%) were reported during the study, with median overall survival time of 19.1 months and an accompanying 95% CI of [10.5 – 26.5].

Cause of death was disease progression in all cases except for one patient whose cause of death was an AE related to a new anti-cancer treatment for disease progression.

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

End point timeframe:

Date of starting treatment and the date of death due to any cause

| End point values | Single Arm | | | |
|----------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 47 ^[3] | | | |
| Units: Months | | | | |
| number (confidence interval 95%) | | | | |
| Median Time to Death | 19.1 (10.5 to 26.5) | | | |

Notes:

[3] - 47 deaths were reported

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs meeting serious criteria were reported up to 30 days after last dose of IMP. AEs or SAEs after 30 days of active follow up deemed to be causally related to IMP during study was forwarded to CTI

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 25.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | Single Arm |
|-----------------------|------------|

Reporting group description:

Phase II single arm study of pazopanib after failure of 1st Line therapy with sunitinib

| Serious adverse events | Single Arm | | |
|---|------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 16 / 54 (29.63%) | | |
| number of deaths (all causes) | 47 | | |
| number of deaths resulting from adverse events | | | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gamma-glutamyltransferase increased | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Circulatory collapse | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Surgical and medical procedures | | | |
| Hernia repair | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Ataxia | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Transient ischaemic attack | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abdominal Pain Upper | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Constipation | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nausea | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------|--|--|
| Vomiting | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary retention | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 3 / 54 (5.56%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Back Pain | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Mobility decreased | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tonsillitis | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | Single Arm | | |
|---|-------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 54 / 54 (100.00%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Pain in lumps in neck and back (soft tissue metastases) | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| New lt buttock lump soft tissue metastasis/nodule) | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Vascular disorders | | | |
| Increase tsh | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Hypertension | | | |
| subjects affected / exposed | 24 / 54 (44.44%) | | |
| occurrences (all) | 34 | | |
| Hypotension | | | |
| subjects affected / exposed | 7 / 54 (12.96%) | | |
| occurrences (all) | 7 | | |
| Surgical and medical procedures | | | |
| Dental extraction gum | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |

| | | | |
|--|------------------------|--|--|
| Tooth removed subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 | | |
| Dental extraction subjects affected / exposed occurrences (all) | 2 / 54 (3.70%) 2 | | |
| Spinal fusion surgery subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 | | |
| Shoulder replacement subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 | | |
| General disorders and administration site conditions | | | |
| Malignant pyrexia subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 | | |
| Fatigue subjects affected / exposed occurrences (all) | 29 / 54 (53.70%) 41 | | |
| Lump in right forearm appears larger subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 | | |
| Tenderness in both feet subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 | | |
| Bilateral leg oedema scattered subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 | | |
| Pyrexia subjects affected / exposed occurrences (all) | 2 / 54 (3.70%) 4 | | |
| Feeling cold subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 | | |
| Swelling rt groin | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Pitting oedema | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Left sided pain radiating to back | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Flu like symptoms | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 2 | | |
| Bipedal oedema | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| chest pain | | | |
| subjects affected / exposed | 4 / 54 (7.41%) | | |
| occurrences (all) | 4 | | |
| Left calf swelling | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Inflammation of left arm post aredia iv | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Mucositis | | | |
| subjects affected / exposed | 6 / 54 (11.11%) | | |
| occurrences (all) | 6 | | |
| Pain | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences (all) | 4 | | |
| Malaise | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Reproductive system and breast disorders | | | |

| | | | |
|--|-----------------------|--|--|
| Blood discharge from penis subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 | | |
| Swollen penis subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 | | |
| Testicular pain subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 | | |
| Intermittant scrotal rash subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Crepes left upper lobe subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 | | |
| Productive cough subjects affected / exposed occurrences (all) | 3 / 54 (5.56%) 3 | | |
| Sore throat subjects affected / exposed occurrences (all) | 4 / 54 (7.41%) 4 | | |
| Cough subjects affected / exposed occurrences (all) | 8 / 54 (14.81%) 11 | | |
| Post nasal drip subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 | | |
| Epistaxis subjects affected / exposed occurrences (all) | 3 / 54 (5.56%) 3 | | |
| Sob on exertion subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 | | |
| Runny nose | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Shortness of breath on exertion | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 6 / 54 (11.11%) | | |
| occurrences (all) | 7 | | |
| Bronchopulmonary hemorrhage | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Wheezes/crackles in right lower base lung | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Pneumonitis | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Haemoptysis | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Lung infection | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 2 | | |
| Bilateral pulmonary embolism | | | |
| subjects affected / exposed | 3 / 54 (5.56%) | | |
| occurrences (all) | 3 | | |
| Pleuretic chest pain | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Hoarse voice | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |

| | | | |
|--|-----------------------|--|--|
| Blocked nose subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 | | |
| Psychiatric disorders | | | |
| Depression subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 | | |
| Insomnia subjects affected / exposed occurrences (all) | 2 / 54 (3.70%) 2 | | |
| Anxiety subjects affected / exposed occurrences (all) | 2 / 54 (3.70%) 2 | | |
| Confusion subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 | | |
| Low mood subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 | | |
| Hallucinations subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 | | |
| Investigations | | | |
| Weight Loss subjects affected / exposed occurrences (all) | 9 / 54 (16.67%) 19 | | |
| hypokalemia subjects affected / exposed occurrences (all) | 2 / 54 (3.70%) 3 | | |
| Raised bilirubin subjects affected / exposed occurrences (all) | 2 / 54 (3.70%) 2 | | |
| Raised upc subjects affected / exposed occurrences (all) | 1 / 54 (1.85%) 1 | | |
| Increase in bp | | | |

| | | | |
|-------------------------------|-----------------|--|--|
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Alkaline phosphatase increase | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences (all) | 4 | | |
| Raised alt | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences (all) | 3 | | |
| Weight gain | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 2 | | |
| Raised creatinine | | | |
| subjects affected / exposed | 9 / 54 (16.67%) | | |
| occurrences (all) | 17 | | |
| Ldh increase | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Glucose increase | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 3 | | |
| Albumin decrease | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 2 | | |
| Phosphate decrease | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 3 | | |
| Rising grade 3 gamma gt | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Decreased magnesium | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences (all) | 2 | | |
| Decreased neutrophilis | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Platlets decrease | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Sodium increase | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Raised crp | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Pleurisy | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences (all) | 2 | | |
| Alt increase | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Hypophosphatemia | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences (all) | 2 | | |
| Abnormal ecg | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Injury, poisoning and procedural complications | | | |
| Pseudoaneurysm | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Wound bleeding lesion left ring finger | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Right leg pain post op | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Incisional hernia | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Pain (hernia repair site | | | |

| | | | |
|--|---|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Fall</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 54 (1.85%)</p> <p>1</p> <p>1 / 54 (1.85%)</p> <p>2</p> | | |
| <p>Congenital, familial and genetic disorders</p> <p>Incidental finding of pfo</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 54 (1.85%)</p> <p>1</p> | | |
| <p>Cardiac disorders</p> <p>Tachycardia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Bradycardia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Asymptomatic lvef</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 54 (1.85%)</p> <p>1</p> <p>2 / 54 (3.70%)</p> <p>2</p> <p>1 / 54 (1.85%)</p> <p>1</p> | | |
| <p>Nervous system disorders</p> <p>Headaches</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Light headedness</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Taste disturbance</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Peripheral neuropathy intermittent</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Memory impairment</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Burning sensation feet</p> | <p>17 / 54 (31.48%)</p> <p>20</p> <p>2 / 54 (3.70%)</p> <p>2</p> <p>3 / 54 (5.56%)</p> <p>3</p> <p>1 / 54 (1.85%)</p> <p>1</p> <p>1 / 54 (1.85%)</p> <p>1</p> | | |

| | | | |
|--------------------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Dizziness | | | |
| subjects affected / exposed | 4 / 54 (7.41%) | | |
| occurrences (all) | 5 | | |
| Sensory neuropathy (fingers) | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Spinal cord compression | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Vasovagal event | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Restless leg syndrome | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Blood and lymphatic system disorders | | | |
| Worsening anemia | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences (all) | 2 | | |
| Neutropenia | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences (all) | 8 | | |
| Iliac lymphadenopathy | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Ear and labyrinth disorders | | | |
| Hearing loss | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Right ear pain | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Ear disorder | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Eye disorders | | | |
| Watery eyes | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Vitreous hemorrhages | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Cyst eye | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Pain in right eye secondary to shingles | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Vision disturbance (flashing) | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Mild periorbital oedema | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Visual disturbance | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 3 | | |
| Gastrointestinal disorders | | | |
| Abdominal cramps | | | |
| subjects affected / exposed | 7 / 54 (12.96%) | | |
| occurrences (all) | 8 | | |
| Heartburn | | | |
| subjects affected / exposed | 3 / 54 (5.56%) | | |
| occurrences (all) | 3 | | |
| Pain in right side abdomen | | | |

| | | | |
|-----------------------------|------------------|--|--|
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 24 / 54 (44.44%) | | |
| occurrences (all) | 74 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 10 / 54 (18.52%) | | |
| occurrences (all) | 11 | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 3 / 54 (5.56%) | | |
| occurrences (all) | 3 | | |
| Tender abdomen | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Constipation | | | |
| subjects affected / exposed | 15 / 54 (27.78%) | | |
| occurrences (all) | 22 | | |
| Ruq tendernes | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Nausea | | | |
| subjects affected / exposed | 17 / 54 (31.48%) | | |
| occurrences (all) | 29 | | |
| Gastric reflux | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Vomiting | | | |
| subjects affected / exposed | 13 / 54 (24.07%) | | |
| occurrences (all) | 19 | | |
| Abdominal bloating | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Dry mouth | | | |

| | | | |
|-----------------------------------|----------------|--|--|
| subjects affected / exposed | 3 / 54 (5.56%) | | |
| occurrences (all) | 3 | | |
| Flatulence | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences (all) | 2 | | |
| Pancreatitis | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Pain abdomen | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Abdominal soreness (gastric pain) | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Gastritis | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences (all) | 2 | | |
| Esophagitis | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Haemorrhoids | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Palpation soreness epigastric | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Belching | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Sore on lips | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Tongue sensitivity | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Sluggish bowel | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Discomfort right upper quadrant | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Stomatitis | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences (all) | 3 | | |
| Pain ruq | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Gastroesophageal reflux | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences (all) | 2 | | |
| Anal pain | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Stomach rumbling | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Upset stomach | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Hepatobiliary disorders | | | |
| Jaundice | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Skin and subcutaneous tissue disorders | | | |
| Skin discolouration nipple area | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Hair colour change | | | |
| subjects affected / exposed | 9 / 54 (16.67%) | | |
| occurrences (all) | 9 | | |
| Small erythematous lesions | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Dry skin on face | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences (all) | 2 | | |
| Dry skin on hands | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Yellow discolouration of skin | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Alopecia | | | |
| subjects affected / exposed | 5 / 54 (9.26%) | | |
| occurrences (all) | 5 | | |
| Dry skin on feet | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Painful callus r foot | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Hfsr | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Palm rash | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Skin rash allergy | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Urticaria skin rash bilateral arms and | | | |

| | | | |
|---|-----------------|--|--|
| legs | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Urticaria to bilateral arms and 2 [degree] to bites | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Rash with itch | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 2 | | |
| Skin rash | | | |
| subjects affected / exposed | 7 / 54 (12.96%) | | |
| occurrences (all) | 8 | | |
| Worsening rash (likely cutaneous lupus) | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Dry skin | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Scalp rash | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Plantar palmar syndrome | | | |
| subjects affected / exposed | 3 / 54 (5.56%) | | |
| occurrences (all) | 6 | | |
| Skin change | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Facial Rash | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 2 | | |
| Hyperkeratosis | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Skin lesion behind (l) ear lobe | | | |

| | | | |
|--------------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Seborrheic dermatitis - face | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Ecchymosis | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Skin changes-facial redness | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Renal and urinary disorders | | | |
| Increase in urine output | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Urinary frequency increase | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Dysuria | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Urinary urgency | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Proteinuria | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences (all) | 3 | | |
| Urine discoloration | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Urine disorders (bilirubin ++) | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Haematuria | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |

| | | | |
|---|------------------|--|--|
| Endocrine disorders | | | |
| Hypothyroidism | | | |
| subjects affected / exposed | 3 / 54 (5.56%) | | |
| occurrences (all) | 3 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Back Pain | | | |
| subjects affected / exposed | 14 / 54 (25.93%) | | |
| occurrences (all) | 18 | | |
| Ankle Swelling | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Calf cramp | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Pain right foot | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Pain right pelvis +leg | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Arthralgia right hip | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| General weakness in leg | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Shoulder pain | | | |
| subjects affected / exposed | 7 / 54 (12.96%) | | |
| occurrences (all) | 8 | | |
| Reduced mobility | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Flank pain | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Painful r foot | | | |

| | | | |
|--------------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Painful lump in inner groin | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Leg & feet cramps intermittent | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Leg cramps | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| groin pain | | | |
| subjects affected / exposed | 3 / 54 (5.56%) | | |
| occurrences (all) | 3 | | |
| Lower limb pain at night | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Arthralgia | | | |
| subjects affected / exposed | 3 / 54 (5.56%) | | |
| occurrences (all) | 3 | | |
| Pain jaw | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences (all) | 3 | | |
| Pain lower limb | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Pain lower back | | | |
| subjects affected / exposed | 3 / 54 (5.56%) | | |
| occurrences (all) | 3 | | |
| Pain to r heel | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Back ache | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Ganglion left wrist | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Lesion to forehead worsening. lytic lesion (skull) | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Left groin discomfort | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| hip pain | | | |
| subjects affected / exposed | 3 / 54 (5.56%) | | |
| occurrences (all) | 4 | | |
| Myalgia | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences (all) | 3 | | |
| Red tender sides of feet | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Lower rib pain | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Rt axilla pain | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 2 | | |
| Rt scapular pain | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 2 | | |
| Osteonecrosis of the jaw | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Pain left knee | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Supraspinatus tendonitis | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |

| | | | |
|-----------------------------|----------------|--|--|
| groin tenderness | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 2 | | |
| General joint stiffness | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Sore right foot | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Sore toe | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Pain in upper right arm | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Infections and infestations | | | |
| Oral thrush | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences (all) | 2 | | |
| Chest infection | | | |
| subjects affected / exposed | 5 / 54 (9.26%) | | |
| occurrences (all) | 6 | | |
| Head cold | | | |
| subjects affected / exposed | 4 / 54 (7.41%) | | |
| occurrences (all) | 4 | | |
| Lrti (slight wheeze + Cough | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Nasal candidiasis | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Oropharyngeal candidiasis | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Candidiasis r axilla | | | |

| | | | |
|---------------------------------|-----------------|--|--|
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 4 / 54 (7.41%) | | |
| occurrences (all) | 4 | | |
| Flu | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences (all) | 2 | | |
| Viral cold | | | |
| subjects affected / exposed | 3 / 54 (5.56%) | | |
| occurrences (all) | 3 | | |
| Buttock abscess | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Glass density in both lungs | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Cutaneous fungal infection | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Shingles | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Leg ulcer infection | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Cystitis | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Rti respiratory tract infection | | | |
| subjects affected / exposed | 6 / 54 (11.11%) | | |
| occurrences (all) | 6 | | |
| Cold sore | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Bronchitis | | | |

| | | | |
|------------------------------------|-----------------|--|--|
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Left basal pneumonia | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Infected right tonsil | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Metabolism and nutrition disorders | | | |
| Anorexia | | | |
| subjects affected / exposed | 8 / 54 (14.81%) | | |
| occurrences (all) | 13 | | |
| Hyponatremia | | | |
| subjects affected / exposed | 3 / 54 (5.56%) | | |
| occurrences (all) | 3 | | |
| Cachectic | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Pain rt shoulder | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Appetite decrease | | | |
| subjects affected / exposed | 5 / 54 (9.26%) | | |
| occurrences (all) | 5 | | |
| Hyperphosphatemia | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Hypermagnesemia | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |
| Dehydration | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences (all) | 2 | | |

| | | | |
|-----------------------------|----------------|--|--|
| Hypercalcaemia | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 2 | | |
| Hyperkalemia | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences (all) | 2 | | |
| Diabetes worsened | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences (all) | 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|--|
| 07 October 2011 | <p>Original Approved Protocol was Protocol V1.0 04Oct2010. It was updated to Protocol V2.0 02Feb2011, but these were non substantial amendments (to edit Data Management procedures for the study including change of group statistician details & some admin changes). This update was submitted with the amendment for Protocol V3.0 21 June 2011.</p> <p>Protocol V3.0 was updated for a number of reasons including to correct requirements for BP levels, changes to Inclusion/Exclusion Criteria/addition of PI at site & removal of a site, Inclusion of planned analysis for the secondary efficacy endpoints, admin changes.</p> <p>Protocol V3.0 was not approved by the Irish Reg Authorities as they requested that a sentence needed to be added regarding Inclusion Criteria after the text on Sunitinib toxicity and eligibility - 'The Investigator should be aware of the patient's Intolerance/Toxicity with prior sunitinib treatment and take this into account when assessing eligibility'.</p> <p>This update resulted in Protocol V4.0 13-Sept-2011 which was approved.</p> |
| 08 October 2013 | <p>Protocol Version 5.0 11-Mar-2013: Principal Changes are:</p> <ul style="list-style-type: none">- Requirement for an extra safety visit to assess liver function at week 6 added in response to updated safety info for pazopanib issued via Dear Investigator Letter.- Change in frequency of CT scans after the 24 week time-point to every 12 weeks (from every 8 weeks) which is in line with Standard of Care- Clarification that Dose Modifications for the managing of treatment related AEs are mandatory as opposed to recommended.- Added recommendations on the use medications that increase gastric pH (PPIs and H2-receptor antagonists) as per IB V10- Clarification in the working of primary & secondary endpoints |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported