



Clinical trial results:

A randomized, open label, multicenter Phase 2/3 study to evaluate the efficacy and safety of rogaratinib (BAY 1163877) compared to chemotherapy in patients with FGFR-positive locally advanced or metastatic urothelial carcinoma who have received prior platinum-containing-chemotherapy

Summary

| | |
|--------------------------|---|
| EudraCT number | 2016-004340-11 |
| Trial protocol | GB IE NL FR AT CZ ES PT FI SK HU DK BE SE PL IT |
| Global end of trial date | 27 October 2020 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 30 October 2021 |
| First version publication date | 30 October 2021 |

Trial information

Trial identification

| | |
|-----------------------|-------|
| Sponsor protocol code | 17403 |
|-----------------------|-------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03410693 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Bayer AG |
| Sponsor organisation address | Kaiser Wilhelm Allee, Leverkusen, Germany, D-51368 |
| Public contact | Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.com |
| Scientific contact | Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.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 | 31 December 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 27 October 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Primary objective for the Phase 2 part of the study was to demonstrate the efficacy of rogaratinib over chemotherapy (docetaxel, paclitaxel, or vinflunine) in terms of ORR of urothelial carcinoma patients with FGFR positive tumors. The original objective of the Phase 3 part of the study was to demonstrate the superiority of rogaratinib over chemotherapy in terms of prolonging the overall survival (OS) of urothelial carcinoma patients with FGFR positive tumors. Once the decision was made to not conduct the Phase 3 part of the study, OS was then considered an exploratory efficacy variable for Phase 2.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki and the International Council for Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent was read by and explained to all the subjects. Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------|
| Actual start date of recruitment | 31 May 2018 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Australia: 9 |
| Country: Number of subjects enrolled | Austria: 3 |
| Country: Number of subjects enrolled | Belgium: 4 |
| Country: Number of subjects enrolled | Canada: 1 |
| Country: Number of subjects enrolled | Switzerland: 5 |
| Country: Number of subjects enrolled | China: 4 |
| Country: Number of subjects enrolled | Czechia: 1 |
| Country: Number of subjects enrolled | Denmark: 4 |
| Country: Number of subjects enrolled | Spain: 16 |
| Country: Number of subjects enrolled | France: 16 |
| Country: Number of subjects enrolled | United Kingdom: 4 |
| Country: Number of subjects enrolled | Hungary: 3 |
| Country: Number of subjects enrolled | Ireland: 6 |
| Country: Number of subjects enrolled | Israel: 4 |

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Italy: 21 |
| Country: Number of subjects enrolled | Japan: 14 |
| Country: Number of subjects enrolled | Korea, Republic of: 15 |
| Country: Number of subjects enrolled | Netherlands: 2 |
| Country: Number of subjects enrolled | Poland: 10 |
| Country: Number of subjects enrolled | Portugal: 5 |
| Country: Number of subjects enrolled | Russian Federation: 6 |
| Country: Number of subjects enrolled | Slovakia: 4 |
| Country: Number of subjects enrolled | Sweden: 1 |
| Country: Number of subjects enrolled | Taiwan: 14 |
| Country: Number of subjects enrolled | United States: 3 |
| Worldwide total number of subjects | 175 |
| EEA total number of subjects | 96 |

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) | 55 |
| From 65 to 84 years | 119 |
| 85 years and over | 1 |

Subject disposition

Recruitment

Recruitment details:

This study enrolled participants at 111 centers in 28 countries from 31 MAY 2018 (first participant first visit) to 27 OCT 2020 (last participant last visit).

Pre-assignment

Screening details:

A total of 718 participants signed the informed consent for prescreening, of which 256 participants completed the prescreening, while 462 participants discontinued the prescreening. The discontinuations were due to screening failure (322), other reasons (98), withdrawal by the participant (22), and death (20).

Period 1

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

Arms

| | |
|------------------------------|---|
| Are arms mutually exclusive? | Yes |
| Arm title | Rogaratinib (BAY1163877)_overall population |

Arm description:

Participants who were randomized to this group following a 1:1 ratio received rogaratinib 600 mg orally twice a day (b.i.d.) continuously, during a 21-day treatment cycle.

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | Rogaratinib |
| Investigational medicinal product code | BAY1163877 |
| Other name | |
| Pharmaceutical forms | Coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Rogaratinib 600 mg (consisting of 3 tablets à 200 mg) was taken orally (p.o.) twice a day (b.i.d.), continuously, during a 21-day treatment cycle.

| | |
|------------------|---------------------------------|
| Arm title | Chemotherapy_overall population |
|------------------|---------------------------------|

Arm description:

Participants who were randomized to this group following a 1:1 ratio received chemotherapy (docetaxel, paclitaxel or vinflunine) at the discretion of the investigator, as intravenous (i.v.) infusion once every three weeks (on day 1 of a 21-day cycle).

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Docetaxel |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

The starting dose for docetaxel was 75 mg/m² given as i.v. infusion, once every three weeks (on day 1 of a 21-day cycle).

| | |
|--|-----------------|
| Investigational medicinal product name | Vinflunine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

The starting dose for vinflunine was 320 mg/m² given as i.v. infusion, once every three weeks (on day 1 of a 21-day cycle).

| | |
|--|-----------------|
| Investigational medicinal product name | Paclitaxel |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

The starting dose for paclitaxel was 175 mg/m² given as i.v. infusion, once every three weeks (on day 1 of a 21-day cycle).

| Number of subjects in period 1 | Rogaratinib (BAY1163877)_over all population | Chemotherapy_over all population |
|---|--|-------------------------------------|
| Started | 87 | 88 |
| Started treatment | 86 | 82 |
| Active follow-up performed | 61 | 56 |
| Entered long term follow-up | 56 | 69 |
| Completed | 0 | 0 |
| Not completed | 87 | 88 |
| Disc trt: Lost to follow up | - | 1 |
| Disc trt: Withdrawal by participant | 6 | 4 |
| Disc trt: radiological progression | 58 | 50 |
| Disc trt:AE not asso. w/ clinical disease progress | 1 | 4 |
| Discontinued (disc) treatment (trt): Death | 6 | 4 |
| Study drug never administered | 1 | 6 |
| Disc trt: clinical progression | 1 | 5 |
| Disc trt: Physician decision | - | 5 |
| Disc trt: Adverse Event (AE) | 13 | 9 |
| Disc trt: Other | 1 | - |

Baseline characteristics

Reporting groups

| | |
|---|---|
| Reporting group title | Rogaratinib (BAY1163877)_overall population |
| Reporting group description: | |
| Participants who were randomized to this group following a 1:1 ratio received rogaratinib 600 mg orally twice a day (b.i.d.) continuously, during a 21-day treatment cycle. | |
| Reporting group title | Chemotherapy_overall population |
| Reporting group description: | |
| Participants who were randomized to this group following a 1:1 ratio received chemotherapy (docetaxel, paclitaxel or vinflunine) at the discretion of the investigator, as intravenous (i.v.) infusion once every three weeks (on day 1 of a 21-day cycle). | |

| Reporting group values | Rogaratinib (BAY1163877)_overall population | Chemotherapy_overall population | Total |
|--|---|---------------------------------|-------|
| Number of subjects | 87 | 88 | 175 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 23 | 32 | 55 |
| From 65-84 years | 64 | 55 | 119 |
| 85 years and over | 0 | 1 | 1 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 67.7 | 66.4 | - |
| standard deviation | ± 8.3 | ± 10.3 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 75 | 70 | 145 |
| Male | 12 | 18 | 30 |
| Race | | | |
| Units: Subjects | | | |
| White | 55 | 55 | 110 |
| Black or African American | 1 | 0 | 1 |
| Asian | 23 | 25 | 48 |
| Not reported | 8 | 8 | 16 |
| Ethnicity | | | |
| Units: Subjects | | | |
| Not Hispanic or Latino | 76 | 78 | 154 |
| Hispanic or Latino | 1 | 0 | 1 |
| Not reported | 10 | 10 | 20 |
| Cancer Category | | | |
| Units: Subjects | | | |

| | | | |
|---|----|----|-----|
| Location of primary cancer: bladder | 56 | 45 | 101 |
| Location of primary cancer: Ureter | 17 | 14 | 31 |
| Location of primary cancer: Renal pelvis | 12 | 28 | 40 |
| Location of primary cancer: Proximal urethra | 2 | 1 | 3 |
| Cancer stage at study entry | | | |
| Units: Subjects | | | |
| Stage III B | 1 | 3 | 4 |
| Stage IV | 5 | 12 | 17 |
| Stage IV A | 13 | 24 | 37 |
| Stage IV B | 67 | 48 | 115 |
| Unknown | 1 | 1 | 2 |
| PIK3CA and/or RAS activating mutations | | | |
| PIK3CA: Phosphoinositide 3 kinase, catalytic subunit alpha isoform RAS: Rat sarcoma | | | |
| Units: Subjects | | | |
| Absent | 65 | 69 | 134 |
| Present | 10 | 10 | 20 |
| Unknown | 12 | 9 | 21 |
| FGFR expression from Targos | | | |
| FGFR: Fibroblast growth factor receptor | | | |
| Units: Subjects | | | |
| Negative | 13 | 14 | 27 |
| Positive | 69 | 69 | 138 |
| Not assessed | 5 | 5 | 10 |

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | Rogaratinib (BAY1163877)_overall population |
| Reporting group description: Participants who were randomized to this group following a 1:1 ratio received rogaratinib 600 mg orally twice a day (b.i.d.) continuously, during a 21-day treatment cycle. | |
| Reporting group title | Chemotherapy_overall population |
| Reporting group description: Participants who were randomized to this group following a 1:1 ratio received chemotherapy (docetaxel, paclitaxel or vinflunine) at the discretion of the investigator, as intravenous (i.v.) infusion once every three weeks (on day 1 of a 21-day cycle). | |
| Subject analysis set title | Rogaratinib_WT population |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Wild type population | |
| Subject analysis set title | Chemotherapy_WT population |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Wild type population | |

Primary: Objective response rate (ORR) - central assessment

| | |
|---|--|
| End point title | Objective response rate (ORR) - central assessment |
| End point description: ORR is defined as the percentage of participants with complete response (CR) or partial response (PR). participants for whom overall best response is not CR or PR, as well as participants without any post-baseline tumor assessment will be considered non-responders. | |
| End point type | Primary |
| End point timeframe: From start of treatment up to end of active follow-up | |

| End point values | Rogaratinib (BAY1163877)_overall population | Chemotherapy_overall population | Rogaratinib_WT population | Chemotherapy_WT population |
|----------------------------------|---|---------------------------------|---------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 87 | 88 | 62 | 63 |
| Units: percentage | | | | |
| number (confidence interval 95%) | 19.5 (11.8 to 29.4) | 21.6 (13.5 to 31.6) | 19.4 (10.4 to 31.4) | 23.8 (14.0 to 36.2) |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | ORR difference_overall population |
| Comparison groups | Rogaratinib (BAY1163877)_overall population v Chemotherapy_overall population |

| | |
|---|----------------------|
| Number of subjects included in analysis | 175 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6991 |
| Method | Fisher exact |
| Parameter estimate | ORR difference (R-C) |
| Point estimate | -2.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -14 |
| upper limit | 9.9 |

| | |
|---|--|
| Statistical analysis title | ORR difference_WT Population |
| Comparison groups | Chemotherapy_WT population v Rogaratinib_WT population |
| Number of subjects included in analysis | 125 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7944 |
| Method | Fisher exact |
| Parameter estimate | ORR difference (R – C) |
| Point estimate | -4.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -18.9 |
| upper limit | 9.9 |

Secondary: Disease-control rate (DCR) - central assessment

| | |
|---|---|
| End point title | Disease-control rate (DCR) - central assessment |
| End point description: | |
| DCR was defined as the percentage of participants whose overall best response was not a progressive disease (i.e., CR, PR, stable disease [SD] or Non CR/Non PD). | |
| End point type | Secondary |
| End point timeframe: | |
| From start of treatment till end of active follow-up | |

| End point values | Rogaratinib (BAY1163877) _overall population | Chemotherapy _overall population | Rogaratinib_W T population | Chemotherapy _WT population |
|----------------------------------|--|----------------------------------|----------------------------|-----------------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 87 | 88 | 62 | 63 |
| Units: percentage | | | | |
| number (confidence interval 95%) | 50.6 (39.6 to | 55.7 (44.7 to | 53.2 (40.1 to | 63.5 (50.4 to |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | DCR difference_Overall Population |
| Comparison groups | Rogaratinib (BAY1163877)_overall population v Chemotherapy_overall population |
| Number of subjects included in analysis | 175 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7962 |
| Method | Fisher exact |
| Parameter estimate | DCR difference (R-C) |
| Point estimate | -5.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -19.9 |
| upper limit | 9.7 |

| | |
|---|--|
| Statistical analysis title | DCR difference_WT population |
| Comparison groups | Rogaratinib_WT population v Chemotherapy_WT population |
| Number of subjects included in analysis | 125 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9109 |
| Method | Fisher exact |
| Parameter estimate | DCR difference (R-C) |
| Point estimate | -10.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -27.5 |
| upper limit | 6.9 |

Secondary: Progression-free survival (PFS) - central assessment

| | |
|------------------------|--|
| End point title | Progression-free survival (PFS) - central assessment |
| End point description: | Progression free survival (PFS) was defined as the time (days) from randomization to date of first observed disease progression (radiological or clinical assessment or both) or death due to any cause (if death occurred before progression was documented). |
| End point type | Secondary |

End point timeframe:

From start of treatment till end of active follow-up

| End point values | Rogaratib (BAY1163877)_overall population | Chemotherapy_overall population | Rogaratib_WT population | Chemotherapy_WT population |
|----------------------------------|---|---------------------------------|-------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 87 | 88 | 62 | 63 |
| Units: months | | | | |
| median (confidence interval 95%) | 2.7 (1.6 to 4.6) | 3.2 (2.7 to 4.4) | 2.8 (2.6 to 5.1) | 4.0 (2.8 to 6.1) |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Hazard ratio (R/C)_Overall population |
| Comparison groups | Rogaratib (BAY1163877)_overall population v Chemotherapy_overall population |
| Number of subjects included in analysis | 175 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8672 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.226 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.853 |
| upper limit | 1.762 |

| | |
|---|--|
| Statistical analysis title | Hazard ratio (R/C)_WT population |
| Comparison groups | Rogaratib_WT population v Chemotherapy_WT population |
| Number of subjects included in analysis | 125 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9171 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.341 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.88 |
| upper limit | 2.043 |

Secondary: Duration of response (DOR)- central assessment

| | |
|-----------------|--|
| End point title | Duration of response (DOR)- central assessment |
|-----------------|--|

End point description:

DOR (for patients with PR and CR only) was defined as the time from the first documented objective response of PR or CR, whichever was noted earlier, to disease progression (including symptomatic deterioration) or death, whichever was earlier

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

End point timeframe:

From start of treatment till end of active follow-up

| End point values | Rogaratinib (BAY1163877) _overall population | Chemotherapy _overall population | Rogaratinib_W T population | Chemotherapy _WT population |
|----------------------------------|---|-------------------------------------|-------------------------------|--------------------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 87 | 88 | 62 | 63 |
| Units: months | | | | |
| median (confidence interval 95%) | 4.9 (2.2 to 7.0) | 5.8 (3.5 to 7.7) | 5.1 (1.5 to 9.2) | 7.0 (2.7 to 8.4) |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with treatment emergent adverse events

| | |
|-----------------|---|
| End point title | Number of participants with treatment emergent adverse events |
|-----------------|---|

End point description:

A treatment-emergent event is defined as any event arising or worsening after the start of study drug administration until 30 days after the last administration of study treatment.

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

End point timeframe:

From start of treatment up to 30 days after the last administration of study treatment

| End point values | Rogaratinib (BAY1163877) _overall population | Chemotherapy _overall population | | |
|-----------------------------|---|-------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 86 | 82 | | |
| Units: participants | | | | |
| Any TEAE | 86 | 82 | | |
| Any drug related TEAE | 81 | 76 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the start of study drug administration until 30 days after the last administration of study treatment

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 23.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------------------|
| Reporting group title | Rogaratinib (BAY1163877) |
|-----------------------|--------------------------|

Reporting group description:

Participants who were randomized to this group following a 1:1 ratio received rogaratinib 600 mg orally twice a day (b.i.d.) continuously, during a 21-day treatment cycle.

| | |
|-----------------------|--------------|
| Reporting group title | Chemotherapy |
|-----------------------|--------------|

Reporting group description:

Participants who were randomized to this group following a 1:1 ratio received chemotherapy (docetaxel, paclitaxel or vinflunine) at the discretion of the investigator, as intravenous (i.v.) infusion once every three weeks (on day 1 of a 21-day cycle).

| Serious adverse events | Rogaratinib (BAY1163877) | Chemotherapy | |
|--|-----------------------------|------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 39 / 86 (45.35%) | 33 / 82 (40.24%) | |
| number of deaths (all causes) | 47 | 45 | |
| number of deaths resulting from adverse events | 16 | 5 | |
| Surgical and medical procedures | | | |
| Ureteral stent insertion | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Condition aggravated | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Death | | | |
| subjects affected / exposed | 4 / 86 (4.65%) | 2 / 82 (2.44%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 4 | 0 / 2 | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General physical health deterioration | | | |
| subjects affected / exposed | 4 / 86 (4.65%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 1 / 6 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 3 | 0 / 1 | |
| Multiple organ dysfunction syndrome | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 3 / 86 (3.49%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 3 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Emphysema | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonitis | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Biopsy liver | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 3 / 7 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Lipase increased | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femoral neck fracture | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hip fracture | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Periprosthetic fracture | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiopulmonary failure | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Nervous system disorders | | | |
| Epilepsy | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic encephalopathy | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Neurotoxicity | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 4 / 82 (4.88%) | |
| occurrences causally related to treatment / all | 0 / 0 | 4 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 4 / 82 (4.88%) | |
| occurrences causally related to treatment / all | 0 / 0 | 6 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |

| | | | |
|---|----------------|----------------|--|
| Abdominal pain | | | |
| subjects affected / exposed | 3 / 86 (3.49%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis ischaemic | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 2 / 82 (2.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inguinal hernia | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal obstruction | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intussusception | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal obstruction | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Volvulus | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic failure | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Anuria | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematuria | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 3 / 82 (3.66%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hydronephrosis | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephritis | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oliguria | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhage urinary tract | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postrenal failure | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract obstruction | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute kidney injury | | | |
| subjects affected / exposed | 3 / 86 (3.49%) | 2 / 82 (2.44%) | |
| occurrences causally related to treatment / all | 3 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal pain | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteonecrosis | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 2 / 82 (2.44%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 2 / 82 (2.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Relapsing fever | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 3 / 82 (3.66%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 86 (1.16%) | 4 / 82 (4.88%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound infection | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urosepsis | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 2 / 82 (2.44%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Groin infection | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Klebsiella infection | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Device related infection | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumocystis jirovecii pneumonia | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia pyelonephritis | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Rogaratinib (BAY1163877) | Chemotherapy | |
|---|-----------------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 85 / 86 (98.84%) | 77 / 82 (93.90%) | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 6 / 86 (6.98%) | 1 / 82 (1.22%) | |
| occurrences (all) | 6 | 1 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 25 / 86 (29.07%) | 19 / 82 (23.17%) | |
| occurrences (all) | 52 | 40 | |

| | | | |
|--|------------------------|------------------------|--|
| Mucosal inflammation subjects affected / exposed occurrences (all) | 7 / 86 (8.14%) 20 | 8 / 82 (9.76%) 12 | |
| Fatigue subjects affected / exposed occurrences (all) | 21 / 86 (24.42%) 32 | 28 / 82 (34.15%) 41 | |
| Oedema peripheral subjects affected / exposed occurrences (all) | 8 / 86 (9.30%) 9 | 10 / 82 (12.20%) 13 | |
| Pyrexia subjects affected / exposed occurrences (all) | 12 / 86 (13.95%) 15 | 10 / 82 (12.20%) 14 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 4 / 86 (4.65%) 6 | 6 / 82 (7.32%) 7 | |
| Dyspnoea subjects affected / exposed occurrences (all) | 3 / 86 (3.49%) 3 | 5 / 82 (6.10%) 6 | |
| Epistaxis subjects affected / exposed occurrences (all) | 10 / 86 (11.63%) 10 | 1 / 82 (1.22%) 1 | |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 5 / 86 (5.81%) 5 | 4 / 82 (4.88%) 4 | |
| Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 13 / 86 (15.12%) 22 | 2 / 82 (2.44%) 4 | |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 10 / 86 (11.63%) 16 | 2 / 82 (2.44%) 3 | |
| Blood creatinine increased subjects affected / exposed occurrences (all) | 11 / 86 (12.79%) 18 | 3 / 82 (3.66%) 6 | |

| | | | |
|--------------------------------------|------------------|------------------|--|
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 5 / 86 (5.81%) | 0 / 82 (0.00%) | |
| occurrences (all) | 6 | 0 | |
| Lipase increased | | | |
| subjects affected / exposed | 9 / 86 (10.47%) | 3 / 82 (3.66%) | |
| occurrences (all) | 25 | 11 | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 14 / 82 (17.07%) | |
| occurrences (all) | 0 | 22 | |
| Weight decreased | | | |
| subjects affected / exposed | 10 / 86 (11.63%) | 6 / 82 (7.32%) | |
| occurrences (all) | 11 | 7 | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 5 / 82 (6.10%) | |
| occurrences (all) | 0 | 5 | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 12 / 86 (13.95%) | 2 / 82 (2.44%) | |
| occurrences (all) | 14 | 3 | |
| Calcium phosphate product increased | | | |
| subjects affected / exposed | 8 / 86 (9.30%) | 0 / 82 (0.00%) | |
| occurrences (all) | 10 | 0 | |
| Nervous system disorders | | | |
| Dysgeusia | | | |
| subjects affected / exposed | 13 / 86 (15.12%) | 5 / 82 (6.10%) | |
| occurrences (all) | 14 | 6 | |
| Headache | | | |
| subjects affected / exposed | 6 / 86 (6.98%) | 4 / 82 (4.88%) | |
| occurrences (all) | 7 | 5 | |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 3 / 86 (3.49%) | 10 / 82 (12.20%) | |
| occurrences (all) | 4 | 12 | |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 10 / 82 (12.20%) | |
| occurrences (all) | 1 | 14 | |
| Blood and lymphatic system disorders | | | |

| | | | |
|---|------------------------|------------------------|--|
| Neutropenia subjects affected / exposed occurrences (all) | 3 / 86 (3.49%) 6 | 19 / 82 (23.17%) 30 | |
| Anaemia subjects affected / exposed occurrences (all) | 11 / 86 (12.79%) 17 | 28 / 82 (34.15%) 66 | |
| Eye disorders | | | |
| Dry eye subjects affected / exposed occurrences (all) | 5 / 86 (5.81%) 5 | 3 / 82 (3.66%) 3 | |
| Detachment of retinal pigment epithelium subjects affected / exposed occurrences (all) | 7 / 86 (8.14%) 16 | 0 / 82 (0.00%) 0 | |
| Subretinal fluid subjects affected / exposed occurrences (all) | 7 / 86 (8.14%) 8 | 0 / 82 (0.00%) 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain subjects affected / exposed occurrences (all) | 15 / 86 (17.44%) 18 | 13 / 82 (15.85%) 27 | |
| Constipation subjects affected / exposed occurrences (all) | 25 / 86 (29.07%) 31 | 29 / 82 (35.37%) 54 | |
| Diarrhoea subjects affected / exposed occurrences (all) | 48 / 86 (55.81%) 92 | 18 / 82 (21.95%) 19 | |
| Dry mouth subjects affected / exposed occurrences (all) | 10 / 86 (11.63%) 15 | 2 / 82 (2.44%) 2 | |
| Mouth ulceration subjects affected / exposed occurrences (all) | 5 / 86 (5.81%) 7 | 3 / 82 (3.66%) 3 | |
| Nausea subjects affected / exposed occurrences (all) | 27 / 86 (31.40%) 38 | 20 / 82 (24.39%) 38 | |
| Vomiting | | | |

| | | | |
|---|------------------------|------------------------|--|
| subjects affected / exposed occurrences (all) | 15 / 86 (17.44%) 19 | 18 / 82 (21.95%) 26 | |
| Stomatitis subjects affected / exposed occurrences (all) | 10 / 86 (11.63%) 15 | 10 / 82 (12.20%) 14 | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia subjects affected / exposed occurrences (all) | 20 / 86 (23.26%) 23 | 24 / 82 (29.27%) 26 | |
| Dry skin subjects affected / exposed occurrences (all) | 7 / 86 (8.14%) 9 | 2 / 82 (2.44%) 2 | |
| Nail discolouration subjects affected / exposed occurrences (all) | 6 / 86 (6.98%) 8 | 0 / 82 (0.00%) 0 | |
| Palmar-plantar erythrodysesthesia syndrome subjects affected / exposed occurrences (all) | 7 / 86 (8.14%) 10 | 0 / 82 (0.00%) 0 | |
| Rash subjects affected / exposed occurrences (all) | 7 / 86 (8.14%) 9 | 3 / 82 (3.66%) 5 | |
| Onychomadesis subjects affected / exposed occurrences (all) | 7 / 86 (8.14%) 8 | 0 / 82 (0.00%) 0 | |
| Nail toxicity subjects affected / exposed occurrences (all) | 7 / 86 (8.14%) 12 | 0 / 82 (0.00%) 0 | |
| Renal and urinary disorders | | | |
| Haematuria subjects affected / exposed occurrences (all) | 9 / 86 (10.47%) 13 | 6 / 82 (7.32%) 8 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 9 / 86 (10.47%) 12 | 7 / 82 (8.54%) 7 | |
| Back pain | | | |

| | | | |
|---|------------------------|------------------------|--|
| subjects affected / exposed occurrences (all) | 8 / 86 (9.30%) 8 | 8 / 82 (9.76%) 9 | |
| Myalgia subjects affected / exposed occurrences (all) | 5 / 86 (5.81%) 6 | 10 / 82 (12.20%) 12 | |
| Pain in extremity subjects affected / exposed occurrences (all) | 7 / 86 (8.14%) 10 | 4 / 82 (4.88%) 4 | |
| Infections and infestations | | | |
| Influenza subjects affected / exposed occurrences (all) | 5 / 86 (5.81%) 5 | 0 / 82 (0.00%) 0 | |
| Conjunctivitis subjects affected / exposed occurrences (all) | 5 / 86 (5.81%) 8 | 3 / 82 (3.66%) 3 | |
| Paronychia subjects affected / exposed occurrences (all) | 7 / 86 (8.14%) 8 | 0 / 82 (0.00%) 0 | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 12 / 86 (13.95%) 12 | 8 / 82 (9.76%) 13 | |
| Metabolism and nutrition disorders | | | |
| Hyperkalaemia subjects affected / exposed occurrences (all) | 8 / 86 (9.30%) 11 | 6 / 82 (7.32%) 14 | |
| Hyperphosphataemia subjects affected / exposed occurrences (all) | 39 / 86 (45.35%) 79 | 0 / 82 (0.00%) 0 | |
| Hyponatraemia subjects affected / exposed occurrences (all) | 6 / 86 (6.98%) 9 | 5 / 82 (6.10%) 7 | |
| Decreased appetite subjects affected / exposed occurrences (all) | 36 / 86 (41.86%) 55 | 21 / 82 (25.61%) 25 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 09 May 2019 | <ul style="list-style-type: none">• The maximum planned dose was reduced to 600 mg BID from 800 mg BID;• The requirement of cytological confirmation of urothelial carcinoma was removed from the inclusion criteria;• A roll over study was introduced;• Post dose 12 lead ECG beyond cycle 5 was removed. |
| 12 November 2019 | <ul style="list-style-type: none">• Clarifications were added to explain that due to the stop of enrollment, the study was not to move forward to its Phase 3 and remain Phase 2;• The primary efficacy variable was updated as ORR for the Phase 2 part, and OS was considered an exploratory efficacy variable for the Phase 2 part;• A post trial access program was added as an option for patients to continue receiving rogaratinib treatment and LPLV to be reached based on the last patient changing to a post trial access program. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported