



Clinical trial results:

A randomized, double-blind, placebo-controlled Phase II-III multi-centre study to evaluate the effect of adjuvant pazopanib (GW786034) versus placebo on post-surgical disease-free survival in patients with stage I non small cell lung cancer and tumor size equal or inferior to 7 cm.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2008-004897-41 |
| Trial protocol | FR |
| Global end of trial date | 01 April 2016 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 10 February 2023 |
| First version publication date | 10 February 2023 |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | IFCT-0703 |
|-----------------------|-----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00775307 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | IFCT |
| Sponsor organisation address | 10 rue de la Grange Batelière , Paris, France, 75009 |
| Public contact | Contact, IFCT, +33 156811045, contact@ifct.fr |
| Scientific contact | Contact, IFCT, +33 156811045, contact@ifct.fr |

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 October 2013 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 01 April 2016 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

To evaluate 'feasibility of regimen' by measuring compliance in patients with once-daily (QD) pazopanib, or placebo, dosed according to protocol, based on the proportion (%) of patients that receive pazopanib, or placebo, for at least 12 weeks within 24 weeks of randomization.

Protection of trial subjects:

Algorithms for management of adverse events were provided in the protocol.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 11 March 2009 |
| 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 | France: 142 |
| Worldwide total number of subjects | 142 |
| EEA total number of subjects | 142 |

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) | 114 |
| From 65 to 84 years | 28 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Between March 2009 and August 2012, 143 patients were randomly assigned, 72 to pazopanib and 71 to placebo, in 29 centers. One patient (pazopanib arm) was ineligible being randomized without consent (and did not receive any treatment) and was excluded from all analyses.

Pre-assignment

Screening details:

Patients (18 to 70 years) with completely resected stage I NSCLC (7th TNM edition), an ECOG performance status of 0 or 1, and adequate hematologic, hepatic, renal, and blood coagulation function were eligible.

Pre-assignment period milestones

| | |
|------------------------------|-----|
| Number of subjects started | 142 |
| Number of subjects completed | 142 |

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor |

Blinding implementation details:

This double-blind, multicenter, phase II/III study assigned by central randomization (1:1, block method)

Arms

| | |
|------------------------------|-----------|
| Are arms mutually exclusive? | Yes |
| Arm title | Pazopanib |

Arm description: -

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

Dosage and administration details:

Pazopanib was administered at 800 or 400 mg once a day.

After 64 patients were included (interim analysis), the independent data monitoring committee (IDMC) recommended reducing the pazopanib dose to 400 mg/day given insufficient compliance.

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description: -

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

Dosage and administration details:

Placebo was administered at 800 or 400 mg once a day.

After 64 patients were included (interim analysis), the independent data monitoring committee (IDMC) recommended reducing the dose to 400 mg/day given insufficient compliance.

| Number of subjects in period 1 | Pazopanib | Placebo |
|---------------------------------------|-----------|---------|
| Started | 71 | 71 |
| Completed | 69 | 69 |
| Not completed | 2 | 2 |
| Physician decision | 1 | 1 |
| Consent withdrawn by subject | 1 | 1 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|-----------|
| Reporting group title | Pazopanib |
| Reporting group description: - | |
| Reporting group title | Placebo |
| Reporting group description: - | |

| Reporting group values | Pazopanib | Placebo | Total |
|---|-----------|----------|-------|
| Number of subjects | 71 | 71 | 142 |
| 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) | | | 0 |
| From 65-84 years | | | 0 |
| 85 years and over | | | 0 |
| Age continuous Units: years | | | |
| median | 57 | 61 | |
| full range (min-max) | 33 to 70 | 44 to 71 | - |
| Gender categorical Units: Subjects | | | |
| Female | 30 | 26 | 56 |
| Male | 41 | 45 | 86 |
| ECOG performance status Units: Subjects | | | |
| PS 0 | 47 | 58 | 105 |
| PS 1 | 24 | 13 | 37 |
| Ethnicity Units: Subjects | | | |
| Caucasian | 69 | 69 | 138 |
| Other | 2 | 2 | 4 |
| Smoking status Units: Subjects | | | |
| Never | 6 | 6 | 12 |
| Current | 13 | 12 | 25 |
| Former | 52 | 52 | 104 |
| Missing | 0 | 1 | 1 |
| Stage Units: Subjects | | | |
| IA | 54 | 59 | 113 |
| IB | 16 | 12 | 28 |

| Missing | 1 | 0 | 1 |
|-------------------------|----|----|-----|
| Histology | | | |
| Units: Subjects | | | |
| Adenocarcinoma | 51 | 56 | 107 |
| Squamous cell carcinoma | 12 | 11 | 23 |
| Other | 8 | 4 | 12 |

End points

End points reporting groups

| | |
|--------------------------------|-----------|
| Reporting group title | Pazopanib |
| Reporting group description: - | |
| Reporting group title | Placebo |
| Reporting group description: - | |

Primary: Compliance rate by planned dose and treatment arm

| | |
|---|--|
| End point title | Compliance rate by planned dose and treatment arm ^[1] |
| End point description: To evaluate 'feasibility of regimen' by measuring compliance in patients with once-daily (QD) pazopanib, or placebo, dosed according to protocol, based on the proportion (%) of patients that receive pazopanib, or placebo, for at least 12 weeks within 24 weeks of randomization. | |
| End point type | Primary |
| End point timeframe: Within 24 weeks of randomization. | |

Notes:

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

Justification: Not available

| End point values | Pazopanib | Placebo | | |
|----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 71 | 71 | | |
| Units: % of patients | | | | |
| number (confidence interval 95%) | | | | |
| 800 mg/day | 38 (23 to 55) | 88 (73 to 96) | | |
| 400 mg/day | 69 (50 to 84) | 93 (77 to 99) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of treatment

| | |
|--|-----------------------|
| End point title | Duration of treatment |
| End point description: | |
| End point type | Secondary |
| End point timeframe: Within 24 weeks of randomization | |

| End point values | Pazopanib | Placebo | | |
|-------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 71 | 71 | | |
| Units: weeks | | | | |
| median (full range (min-max)) | | | | |
| 800 mg/day | 7.2 (0.3 to 26.0) | 24.1 (0.3 to 26.4) | | |
| 400 mg/day | 22.6 (0.7 to 26.6) | 24.3 (0.3 to 26.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Dose modification

| | |
|----------------------------------|-------------------|
| End point title | Dose modification |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Within 24 weeks of randomization | |

| End point values | Pazopanib | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 71 | 71 | | |
| Units: Number of patients | | | | |
| 800 mg/day | 16 | 2 | | |
| 400 mg/day | 12 | 2 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of dose modification

| | |
|------------------------------------|-----------------------------|
| End point title | Number of dose modification |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Within 24 weeks from randomization | |

| End point values | Pazopanib | Placebo | | |
|--------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 71 | 71 | | |
| Units: Number of patients | | | | |
| 800 mg/day : 1 dose reduction | 13 | 12 | | |
| 800 mg/day : 2 dose reductions | 3 | 2 | | |
| 400 mg/day : 1 dose reduction | 2 | 0 | | |
| 400 mg/day :2 dose reductions | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of life

| | |
|------------------------------------|-----------------|
| End point title | Quality of life |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Within 24 weeks from randomization | |

| End point values | Pazopanib | Placebo | | |
|----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 71 | 71 | | |
| Units: Pourcentage | | | | |
| arithmetic mean (standard error) | | | | |
| Global Health Status : baseline | 64.9 (± 17.4) | 67.8 (± 20.5) | | |
| Global Health Status : W12 | 63.2 (± 20.3) | 72.7 (± 18.1) | | |
| Global Health Status : W24 | 64.1 (± 20.1) | 68.6 (± 23.1) | | |
| Physical functioning : baseline | 84.4 (± 12.8) | 83.2 (± 15.0) | | |
| Physical functioning : W12 | 81.0 (± 15.6) | 84.4 (± 14.5) | | |
| Physical functioning : W24 | 86.4 (± 13.4) | 86.1 (± 12.0) | | |
| Fatigue : baseline | 31.3 (± 22.8) | 32.4 (± 23.8) | | |
| Fatigue : W12 | 32.3 (± 23.2) | 27.1 (± 25.6) | | |
| Fatigue : W24 | 31.6 (± 25.9) | 23.8 (± 21.9) | | |
| Nausea and vomiting : baseline | 3.5 (± 9.6) | 5.4 (± 11.8) | | |
| Nausea and vomiting : W12 | 7.0 (± 16.7) | 8.2 (± 15.3) | | |
| Nausea and vomiting : W24 | 9.6 (± 17.1) | 4.3 (± 12.3) | | |
| Dyspnoea : baseline | 24.2 (± 18.5) | 25.5 (± 20.7) | | |
| Dyspnoea : W12 | 24.2 (± 22.9) | 23.6 (± 21.2) | | |
| Dyspnoea : W24 | 26.4 (± 22.7) | 25.4 (± 20.8) | | |
| Pain in chest : baseline | 18.8 (± 27.4) | 20.6 (± 23.8) | | |
| Pain in chest : W12 | 17.1 (± 24.9) | 20.8 (± 24.5) | | |
| Pain in chest : W24 | 14.7 (± 21.7) | 14.6 (± 19.3) | | |

Statistical analyses

No statistical analyses for this end point

Post-hoc: Quality of blinding - Treatment guess by patient

| | |
|-----------------|--|
| End point title | Quality of blinding - Treatment guess by patient |
|-----------------|--|

End point description:

| | |
|----------------|----------|
| End point type | Post-hoc |
|----------------|----------|

End point timeframe:

Up to 47 months

| End point values | Pazopanib | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 69 | 69 | | |
| Units: Number of patients | | | | |
| Placebo | 3 | 32 | | |
| Pazopanib | 61 | 29 | | |
| Missing | 5 | 8 | | |

Statistical analyses

No statistical analyses for this end point

Post-hoc: Quality of blinding - Treatment guess by investigator

| | |
|-----------------|---|
| End point title | Quality of blinding - Treatment guess by investigator |
|-----------------|---|

End point description:

| | |
|----------------|----------|
| End point type | Post-hoc |
|----------------|----------|

End point timeframe:

Up to 47 months

| End point values | Pazopanib | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 69 | 69 | | |
| Units: Number of patients | | | | |
| Placebo | 5 | 48 | | |
| Pazopanib | 62 | 15 | | |
| Missing | 2 | 6 | | |

Statistical analyses

No statistical analyses for this end point

Post-hoc: Quality of blinding - Concordance between patients' and clinicians' guess of treatment

| | |
|-----------------|--|
| End point title | Quality of blinding - Concordance between patients' and clinicians' guess of treatment |
|-----------------|--|

End point description:

| | |
|----------------|----------|
| End point type | Post-hoc |
|----------------|----------|

End point timeframe:

Up to 47 weeks

| End point values | Pazopanib | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 64 | 56 | | |
| Units: Number of patients | | | | |
| Yes | 5 | 17 | | |
| No | 59 | 39 | | |

Statistical analyses

No statistical analyses for this end point

Post-hoc: 5-year overall survival

| | |
|-----------------|-------------------------|
| End point title | 5-year overall survival |
|-----------------|-------------------------|

End point description:

| | |
|----------------|----------|
| End point type | Post-hoc |
|----------------|----------|

End point timeframe:

Up to 47 months

| End point values | Pazopanib | Placebo | | |
|----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 71 | 71 | | |
| Units: % of patients | | | | |
| number (confidence interval 95%) | 83 (72 to 94) | 94 (88 to 100) | | |

Statistical analyses

No statistical analyses for this end point

Post-hoc: Three-year Recurrence-Free Survival

| | |
|------------------------|-------------------------------------|
| End point title | Three-year Recurrence-Free Survival |
| End point description: | |
| End point type | Post-hoc |
| End point timeframe: | |
| Up to 47 months | |

| End point values | Pazopanib | Placebo | | |
|----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 71 | 71 | | |
| Units: % of patients | | | | |
| number (confidence interval 95%) | 76 (65 to 86) | 83 (74 to 92) | | |

Statistical analyses

No statistical analyses for this end point

Post-hoc: Second primary cancers

| | |
|------------------------|------------------------|
| End point title | Second primary cancers |
| End point description: | |
| End point type | Post-hoc |
| End point timeframe: | |
| Up to 47 patients | |

| End point values | Pazopanib | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 71 | 71 | | |
| Units: Number of patients | | | | |
| 800 mg/day | 8 | 3 | | |
| 400 mg/day | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected for a patient from the date of signature of inform consent form, during treatment period and until 30 days after the last dose of study treatment. Deaths were collected until data analysis.

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 18.0 |

Reporting groups

| | |
|--------------------------------|--------------------------------------|
| Reporting group title | Safety population - Pazopanib 800 mg |
| Reporting group description: - | |
| Reporting group title | Safety population - Placebo 800 mg |
| Reporting group description: - | |
| Reporting group title | Safety population - Pazopanib 400 mg |
| Reporting group description: - | |
| Reporting group title | Safety population - Placebo 400 mg |
| Reporting group description: - | |

| Serious adverse events | Safety population - Pazopanib 800 mg | Safety population - Placebo 800 mg | Safety population - Pazopanib 400 mg |
|---|--------------------------------------|------------------------------------|--------------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 2 / 41 (4.88%) | 4 / 32 (12.50%) |
| number of deaths (all causes) | 6 | 1 | 1 |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Fracture | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 41 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fall | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 41 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Cardiac disorder | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 41 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 41 (2.44%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pericarditis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 41 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Loss of consciousness | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 41 (2.44%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Convulsion | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 41 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Malaise | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 41 (2.44%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reduced general condition | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 41 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fever | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 41 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Social circumstances | | | |
| Pregnancy of partner | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 41 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 41 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 41 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bloody diarrhea | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 41 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 41 (2.44%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 41 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Hepatic cytolysis | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 41 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Proteinuria | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 41 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 41 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Anorexia | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 41 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---------------------------------------|--|--|
| Serious adverse events | Safety population - Placebo 400 mg | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | | |
| number of deaths (all causes) | 1 | | |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Fracture | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Fall | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Cardiac disorder | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pericardial effusion | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pericarditis | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Loss of consciousness | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Convulsion | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Malaise | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reduced general condition | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Fever | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Social circumstances | | | |
| Pregnancy of partner | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------|--|--|
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bloody diarrhea | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Hepatic cytolysis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Anorexia | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Safety population - Pazopanib 800 mg | Safety population - Placebo 800 mg | Safety population - Pazopanib 400 mg |
|---|--------------------------------------|------------------------------------|--------------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 38 / 39 (97.44%) | 39 / 41 (95.12%) | 31 / 32 (96.88%) |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 21 / 39 (53.85%) | 11 / 41 (26.83%) | 16 / 32 (50.00%) |
| occurrences (all) | 21 | 11 | 16 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 23 / 39 (58.97%) | 19 / 41 (46.34%) | 26 / 32 (81.25%) |
| occurrences (all) | 23 | 19 | 26 |
| Fever | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 4 / 41 (9.76%) | 4 / 32 (12.50%) |
| occurrences (all) | 1 | 4 | 4 |
| Pain | | | |
| subjects affected / exposed | 22 / 39 (56.41%) | 19 / 41 (46.34%) | 24 / 32 (75.00%) |
| occurrences (all) | 22 | 19 | 24 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Haemorrhage nose | | | |
| subjects affected / exposed | 5 / 39 (12.82%) | 1 / 41 (2.44%) | 2 / 32 (6.25%) |
| occurrences (all) | 5 | 1 | 2 |
| Cough | | | |
| subjects affected / exposed | 13 / 39 (33.33%) | 16 / 41 (39.02%) | 10 / 32 (31.25%) |
| occurrences (all) | 13 | 16 | 10 |

| | | | |
|--|------------------------|------------------------|------------------------|
| Dyspnea subjects affected / exposed occurrences (all) | 12 / 39 (30.77%) 12 | 19 / 41 (46.34%) 19 | 15 / 32 (46.88%) 15 |
| Voice change subjects affected / exposed occurrences (all) | 3 / 39 (7.69%) 3 | 2 / 41 (4.88%) 2 | 2 / 32 (6.25%) 2 |
| Psychiatric disorders | | | |
| Insomnia subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 9 / 41 (21.95%) 9 | 5 / 32 (15.63%) 5 |
| Mood altered subjects affected / exposed occurrences (all) | 5 / 39 (12.82%) 5 | 4 / 41 (9.76%) 4 | 6 / 32 (18.75%) 6 |
| Irritability subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 41 (0.00%) 0 | 1 / 32 (3.13%) 1 |
| Investigations | | | |
| Weight loss subjects affected / exposed occurrences (all) | 3 / 39 (7.69%) 3 | 0 / 41 (0.00%) 0 | 1 / 32 (3.13%) 1 |
| Alanine aminotransferase subjects affected / exposed occurrences (all) | 17 / 39 (43.59%) 17 | 12 / 41 (29.27%) 12 | 17 / 32 (53.13%) 17 |
| Aspartate aminotransferase subjects affected / exposed occurrences (all) | 18 / 39 (46.15%) 18 | 14 / 41 (34.15%) 14 | 10 / 32 (31.25%) 10 |
| Alkaline phosphatase subjects affected / exposed occurrences (all) | 6 / 39 (15.38%) 6 | 7 / 41 (17.07%) 7 | 5 / 32 (15.63%) 5 |
| Bicarbonate serum-low subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 3 / 41 (7.32%) 3 | 0 / 32 (0.00%) 0 |
| Bilirubin subjects affected / exposed occurrences (all) | 9 / 39 (23.08%) 9 | 7 / 41 (17.07%) 7 | 6 / 32 (18.75%) 6 |
| Cholesterol | | | |

| | | | |
|---|------------------------|------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 9 / 39 (23.08%) 9 | 15 / 41 (36.59%) 15 | 13 / 32 (40.63%) 13 |
| Creatinine subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 4 / 41 (9.76%) 4 | 2 / 32 (6.25%) 2 |
| Gamma-glutamyltransferase subjects affected / exposed occurrences (all) | 15 / 39 (38.46%) 15 | 16 / 41 (39.02%) 16 | 12 / 32 (37.50%) 12 |
| Nervous system disorders | | | |
| Dizziness subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 6 / 41 (14.63%) 6 | 1 / 32 (3.13%) 1 |
| Headache subjects affected / exposed occurrences (all) | 11 / 39 (28.21%) 11 | 6 / 41 (14.63%) 6 | 11 / 32 (34.38%) 11 |
| Memory impairment subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 2 / 41 (4.88%) 2 | 0 / 32 (0.00%) 0 |
| Neuropathy-sensory subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 4 / 41 (9.76%) 4 | 1 / 32 (3.13%) 1 |
| Blood and lymphatic system disorders | | | |
| Haemoglobin subjects affected / exposed occurrences (all) | 7 / 39 (17.95%) 7 | 9 / 41 (21.95%) 9 | 5 / 32 (15.63%) 5 |
| Leukocyte subjects affected / exposed occurrences (all) | 3 / 39 (7.69%) 3 | 0 / 41 (0.00%) 0 | 3 / 32 (9.38%) 3 |
| Lymphopenia subjects affected / exposed occurrences (all) | 3 / 39 (7.69%) 3 | 3 / 41 (7.32%) 3 | 2 / 32 (6.25%) 2 |
| Neutrophil subjects affected / exposed occurrences (all) | 5 / 39 (12.82%) 5 | 4 / 41 (9.76%) 4 | 9 / 32 (28.13%) 9 |
| Platelet | | | |

| | | | |
|--|---------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 3 / 39 (7.69%) 3 | 1 / 41 (2.44%) 1 | 7 / 32 (21.88%) 7 |
| Eye disorders | | | |
| Blurred vision | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 41 (0.00%) | 4 / 32 (12.50%) |
| occurrences (all) | 2 | 0 | 4 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 15 / 39 (38.46%) | 5 / 41 (12.20%) | 10 / 32 (31.25%) |
| occurrences (all) | 15 | 5 | 10 |
| Anorexia | | | |
| subjects affected / exposed | 16 / 39 (41.03%) | 5 / 41 (12.20%) | 8 / 32 (25.00%) |
| occurrences (all) | 16 | 5 | 8 |
| Constipation | | | |
| subjects affected / exposed | 4 / 39 (10.26%) | 5 / 41 (12.20%) | 2 / 32 (6.25%) |
| occurrences (all) | 4 | 5 | 2 |
| Diarrhoea | | | |
| subjects affected / exposed | 24 / 39 (61.54%) | 11 / 41 (26.83%) | 21 / 32 (65.63%) |
| occurrences (all) | 24 | 1 | 21 |
| Dysguesia | | | |
| subjects affected / exposed | 9 / 39 (23.08%) | 2 / 41 (4.88%) | 3 / 32 (9.38%) |
| occurrences (all) | 9 | 2 | 3 |
| Flatulence | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 1 / 41 (2.44%) | 0 / 32 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 41 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Mucositis stomatitis | | | |
| subjects affected / exposed | 5 / 39 (12.82%) | 2 / 41 (4.88%) | 3 / 32 (9.38%) |
| occurrences (all) | 5 | 2 | 3 |
| Nausea | | | |
| subjects affected / exposed | 18 / 39 (46.15%) | 5 / 41 (12.20%) | 14 / 32 (43.75%) |
| occurrences (all) | 18 | 5 | 14 |
| Vomiting | | | |

| | | | |
|--|------------------------|----------------------|------------------------|
| subjects affected / exposed occurrences (all) | 10 / 39 (25.64%) 10 | 7 / 41 (17.07%) 7 | 9 / 32 (28.13%) 9 |
| Gastrointestinal haemorrhage subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 41 (0.00%) 0 | 1 / 32 (3.13%) 1 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia subjects affected / exposed occurrences (all) | 5 / 39 (12.82%) 5 | 1 / 41 (2.44%) 1 | 9 / 32 (28.13%) 9 |
| Dry skin subjects affected / exposed occurrences (all) | 5 / 39 (12.82%) 5 | 1 / 41 (2.44%) 1 | 1 / 32 (3.13%) 1 |
| Erythema multiforme subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 1 / 41 (2.44%) 1 | 1 / 32 (3.13%) 1 |
| Hand foot skin reaction subjects affected / exposed occurrences (all) | 4 / 39 (10.26%) 4 | 0 / 41 (0.00%) 0 | 2 / 32 (6.25%) 2 |
| Hyperpigmentation subjects affected / exposed occurrences (all) | 1 / 39 (2.56%) 1 | 2 / 41 (4.88%) 2 | 0 / 32 (0.00%) 0 |
| Hypopigmentation subjects affected / exposed occurrences (all) | 13 / 39 (33.33%) 13 | 2 / 41 (4.88%) 2 | 19 / 32 (59.38%) 19 |
| Pruritus subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 3 / 41 (7.32%) 3 | 2 / 32 (6.25%) 2 |
| Rash subjects affected / exposed occurrences (all) | 8 / 39 (20.51%) 8 | 6 / 41 (14.63%) 6 | 5 / 32 (15.63%) 5 |
| Ulceration subjects affected / exposed occurrences (all) | 2 / 39 (5.13%) 2 | 3 / 41 (7.32%) 3 | 2 / 32 (6.25%) 2 |
| Dermatitis subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 41 (0.00%) 0 | 2 / 32 (6.25%) 2 |

| | | | |
|---|------------------|------------------|------------------|
| Renal and urinary disorders | | | |
| Haemoglobinuria | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 1 / 41 (2.44%) | 0 / 32 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 2 / 41 (4.88%) | 2 / 32 (6.25%) |
| occurrences (all) | 3 | 2 | 2 |
| Proteinuria | | | |
| subjects affected / exposed | 19 / 39 (48.72%) | 16 / 41 (39.02%) | 10 / 32 (31.25%) |
| occurrences (all) | 19 | 16 | 10 |
| Endocrine disorders | | | |
| Hot flashes | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 3 / 41 (7.32%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Hyperthyroidism | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 2 / 41 (4.88%) | 0 / 32 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Hypothyroidism | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 2 / 41 (4.88%) | 1 / 32 (3.13%) |
| occurrences (all) | 1 | 2 | 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 5 / 39 (12.82%) | 1 / 41 (2.44%) | 3 / 32 (9.38%) |
| occurrences (all) | 5 | 1 | 3 |
| Metabolism and nutrition disorders | | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 12 / 39 (30.77%) | 18 / 41 (43.90%) | 10 / 32 (31.25%) |
| occurrences (all) | 12 | 18 | 10 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 5 / 41 (12.20%) | 4 / 32 (12.50%) |
| occurrences (all) | 2 | 5 | 4 |
| Hypertriglyceridemia | | | |
| subjects affected / exposed | 14 / 39 (35.90%) | 21 / 41 (51.22%) | 22 / 32 (68.75%) |
| occurrences (all) | 14 | 21 | 22 |
| Hyperuricemia | | | |

| | | | |
|-----------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed | 3 / 39 (7.69%) | 3 / 41 (7.32%) | 8 / 32 (25.00%) |
| occurrences (all) | 3 | 3 | 8 |
| Hypoalbuminemia | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 3 / 41 (7.32%) | 0 / 32 (0.00%) |
| occurrences (all) | 3 | 3 | 0 |
| Hypocalcemia | | | |
| subjects affected / exposed | 4 / 39 (10.26%) | 3 / 41 (7.32%) | 3 / 32 (9.38%) |
| occurrences (all) | 4 | 3 | 3 |
| Hypoglycemia | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 3 / 41 (7.32%) | 1 / 32 (3.13%) |
| occurrences (all) | 1 | 3 | 1 |
| Hyponatremia | | | |
| subjects affected / exposed | 2 / 39 (5.13%) | 2 / 41 (4.88%) | 3 / 32 (9.38%) |
| occurrences (all) | 2 | 2 | 3 |
| Hypophosphatemia | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 3 / 41 (7.32%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 3 | 1 |

| Non-serious adverse events | Safety population - Placebo 400 mg | | |
|---|---------------------------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 29 / 30 (96.67%) | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 15 / 30 (50.00%) | | |
| occurrences (all) | 15 | | |
| Fever | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pain | | | |
| subjects affected / exposed | 22 / 30 (73.33%) | | |
| occurrences (all) | 22 | | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|------------------------|--|--|
| Haemorrhage nose subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 2 | | |
| Cough subjects affected / exposed occurrences (all) | 14 / 30 (46.67%) 14 | | |
| Dyspnea subjects affected / exposed occurrences (all) | 10 / 30 (33.33%) 10 | | |
| Voice change subjects affected / exposed occurrences (all) | 1 / 30 (3.33%) 1 | | |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 5 / 30 (16.67%) 5 | | |
| Mood altered subjects affected / exposed occurrences (all) | 5 / 30 (16.67%) 5 | | |
| Irritability subjects affected / exposed occurrences (all) | 3 / 30 (10.00%) 3 | | |
| Investigations Weight loss subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | | |
| Alanine aminotransferase subjects affected / exposed occurrences (all) | 4 / 30 (13.33%) 4 | | |
| Aspartate aminotransferase subjects affected / exposed occurrences (all) | 5 / 30 (16.67%) 5 | | |
| Alkaline phosphatase subjects affected / exposed occurrences (all) | 3 / 30 (10.00%) 3 | | |
| Bicarbonate serum-low | | | |

| | | | |
|--------------------------------------|------------------|--|--|
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Bilirubin | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| Cholesterol | | | |
| subjects affected / exposed | 15 / 30 (50.00%) | | |
| occurrences (all) | 15 | | |
| Creatinine | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences (all) | 1 | | |
| Gamma-glutamyltransferase | | | |
| subjects affected / exposed | 11 / 30 (36.67%) | | |
| occurrences (all) | 11 | | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 4 / 30 (13.33%) | | |
| occurrences (all) | 4 | | |
| Headache | | | |
| subjects affected / exposed | 5 / 30 (16.67%) | | |
| occurrences (all) | 5 | | |
| Memory impairment | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| Neuropathy-sensory | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences (all) | 1 | | |
| Blood and lymphatic system disorders | | | |
| Haemoglobin | | | |
| subjects affected / exposed | 5 / 30 (16.67%) | | |
| occurrences (all) | 5 | | |
| Leukocyte | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences (all) | 1 | | |
| Lymphopenia | | | |

| | | | |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| Neutrophil | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| Platelet | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences (all) | 1 | | |
| Eye disorders | | | |
| Blurred vision | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| Anorexia | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| Constipation | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | | |
| occurrences (all) | 3 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 8 / 30 (26.67%) | | |
| occurrences (all) | 8 | | |
| Dysguesia | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Flatulence | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastritis | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| Mucositis stomatitis | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nausea | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | | |
| occurrences (all) | 3 | | |
| Vomiting | | | |
| subjects affected / exposed | 5 / 30 (16.67%) | | |
| occurrences (all) | 5 | | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | | |
| occurrences (all) | 3 | | |
| Dry skin | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| Erythema multiforme | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hand foot skin reaction | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences (all) | 1 | | |
| Hyperpigmentation | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypopigmentation | | | |
| subjects affected / exposed | 4 / 30 (13.33%) | | |
| occurrences (all) | 4 | | |
| Pruritus | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| Rash | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | | |
| occurrences (all) | 3 | | |

| | | | |
|---|----------------------|--|--|
| Ulceration subjects affected / exposed occurrences (all) | 1 / 30 (3.33%) 1 | | |
| Dermatitis subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 2 | | |
| Renal and urinary disorders Haemoglobinuria subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | | |
| Hypercalcaemia subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 2 | | |
| Proteinuria subjects affected / exposed occurrences (all) | 3 / 30 (10.00%) 3 | | |
| Endocrine disorders Hot flashes subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | | |
| Hyperthyroidism subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 2 | | |
| Hypothyroidism subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 2 | | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 1 / 30 (3.33%) 1 | | |
| Metabolism and nutrition disorders Hyperglycaemia subjects affected / exposed occurrences (all) | 9 / 30 (30.00%) 9 | | |
| Hyperkalaemia | | | |

| | | | |
|-----------------------------|------------------|--|--|
| subjects affected / exposed | 4 / 30 (13.33%) | | |
| occurrences (all) | 4 | | |
| Hypertriglyceridemia | | | |
| subjects affected / exposed | 16 / 30 (53.33%) | | |
| occurrences (all) | 16 | | |
| Hyperuricemia | | | |
| subjects affected / exposed | 7 / 30 (23.33%) | | |
| occurrences (all) | 7 | | |
| Hypoalbuminemia | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | | |
| occurrences (all) | 3 | | |
| Hypocalcemia | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| Hypoglycemia | | | |
| subjects affected / exposed | 4 / 30 (13.33%) | | |
| occurrences (all) | 4 | | |
| Hyponatremia | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences (all) | 1 | | |
| Hypophosphatemia | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | | |
| occurrences (all) | 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 26 November 2008 | Clarify recurrence or second cancer. |
| 23 March 2009 | Make minor correction to the protocol and update according to the new investigator brochure. |
| 19 October 2009 | Update IFCT address. |
| 10 March 2010 | Make minor correction to the protocol and update according to the new investigator brochure. |
| 22 October 2010 | Update statistical section following recommendations of the independent data monitoring committee (IDMC) to perform ITT analyses. |
| 29 December 2010 | Reduce the pazopanib dose to 400 mg/day given insufficient compliance as recommended by IDMC and increase the number of inclusions as the recruitment of 31 additional patients in each arm is necessary to evaluate compliance. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/28327934>