



Clinical trial results:

A Phase 2, multicenter, open-label study of BGJ398 in patients with recurrent resectable or unresectable glioblastoma

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2013-002200-13 |
| Trial protocol | IT NL ES BE DE |
| Global end of trial date | 03 October 2018 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 17 October 2019 |
| First version publication date | 17 October 2019 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | BGJ398X2201 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01975701 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Novartis Pharmaceuticals |
| Sponsor organisation address | CH-4002, Basel, Switzerland, |
| Public contact | clinical disclosure office, Novartis Pharma, 41 613241111, novartis.email@novartis.com |
| Scientific contact | Study Director, Novartis Pharmaceuticals, 41 613241111, novartis.email@novartis.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 | 03 October 2018 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 03 October 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

the main objective for this trial was to assess the anti-tumor activity of BGJ398 for patients with GBM and/or other glioma subtypes with FGFR1-TACC1, FGFR3-TACC3 fusion and/or activating mutation in FGFR1,2 or 3, based on progression-free survival rate at 6 month (PFS6)

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 09 December 2013 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Belgium: 1 |
| Country: Number of subjects enrolled | Netherlands: 2 |
| Country: Number of subjects enrolled | Spain: 4 |
| Country: Number of subjects enrolled | Switzerland: 3 |
| Country: Number of subjects enrolled | United States: 16 |
| Worldwide total number of subjects | 26 |
| EEA total number of subjects | 7 |

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) | 21 |
| From 65 to 84 years | 5 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

All 26 patients included were enrolled in the non Surgical arm.

Note : Australia participated in this trial, however no patients received treatment.

Pre-assignment

Screening details: -

Pre-assignment period milestones

| | |
|------------------------------|----|
| Number of subjects started | 26 |
| Number of subjects completed | 26 |

Period 1

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

Arms

| | |
|-----------|---------------------|
| Arm title | BGJ398 non surgical |
|-----------|---------------------|

Arm description:

125 mg BGJ398 non surgical

| | |
|--|---------------|
| Arm type | experimental |
| Investigational medicinal product name | BGJ398 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

BGJ398 25 mg

BGJ398 100 mg

hard gelatin capsules for oral use

| | |
|---------------------------------------|---------------------|
| Number of subjects in period 1 | BGJ398 non surgical |
| Started | 26 |
| Completed | 1 |
| Not completed | 25 |
| Adverse event, serious fatal | 23 |
| Physician decision | 1 |
| Lost to follow-up | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------------------|
| Reporting group title | BGJ398 non surgical |
|-----------------------|---------------------|

Reporting group description:

125 mg BGJ398 non surgical

| Reporting group values | BGJ398 non surgical | Total | |
|--|---------------------|-------|--|
| Number of subjects | 26 | 26 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 21 | 21 | |
| From 65-84 years | 5 | 5 | |
| 85 years and over | 0 | 0 | |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 53.7 | | |
| standard deviation | ± 13.59 | - | |
| Sex: Female, Male | | | |
| Units: Subjects | | | |
| Female | 10 | 10 | |
| Male | 16 | 16 | |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| caucasian | 26 | 26 | |

End points

End points reporting groups

| | |
|--|---------------------|
| Reporting group title | BGJ398 non surgical |
| Reporting group description: 125 mg BGJ398 non surgical | |

Primary: progression free survival

| | |
|---|--|
| End point title | progression free survival ^[1] |
| End point description: To assess the anti-tumor activity of BGJ398 for patients with GBM and/or other glioma subtypes that harbor FGFR1-TACC1, FGFR3-TACC3 fusion and/or activating mutation in FGFR1, 2 or 3 based on PFS6 (PFS rate at 6 months as defined by RANO criteria as assessed by the investigator) | |
| End point type | Primary |
| End point timeframe: 6 months | |

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: no Analysis was performed

| End point values | BGJ398 non surgical | | | |
|----------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 24 | | | |
| Units: months | | | | |
| median (confidence interval 95%) | 1.7 (1.05 to 2.80) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall response rate

| | |
|---|-----------------------|
| End point title | Overall response rate |
| End point description: To further assess the anti-tumor activity of BGJ398 for patients with GBM with an amplification, translocation, or activating mutation in FGFR1,2,3 or 4, based on Objective Response Rate (ORR - patients with measurable disease - as defined by RANO criteria as assessed by the investigator) | |
| End point type | Secondary |
| End point timeframe: 8 months after last patient last visit | |

| | | | | |
|-----------------------------|---------------------|--|--|--|
| End point values | BGJ398 non surgical | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 26 | | | |
| Units: participants | | | | |
| partial response | 2 | | | |
| stable disease | 7 | | | |
| progressive disease | 13 | | | |
| unknown | 3 | | | |
| missing | 1 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

| | |
|---|------------------|
| End point title | Overall survival |
| End point description: | |
| To further assess the anti-tumor activity of BGJ398 for patients with GBM and/or other glioma subtypes that harbor FGFR1-TACC1, FGFR3-TACC3 fusion and/or activating mutation in FGFR1, 2 and 3 based on Overall Survival | |
| End point type | Secondary |
| End point timeframe: | |
| 8 months after LPLV | |

| | | | | |
|----------------------------------|----------------------|--|--|--|
| End point values | BGJ398 non surgical | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 26 | | | |
| Units: months | | | | |
| median (confidence interval 95%) | 6.74 (4.17 to 11.73) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: safety and tolerability

| | |
|--|-------------------------|
| End point title | safety and tolerability |
| End point description: | |
| Safety: type, frequency, and severity of AEs and SAEs; Tolerability: dose interruptions, reductions and dose intensity, and evaluations of laboratory values | |
| End point type | Secondary |
| End point timeframe: | |
| 8 months after LPLV | |

| | | | | |
|--------------------------------------|---------------------|--|--|--|
| End point values | BGJ398 non surgical | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 26 | | | |
| Units: participants | | | | |
| participants with dose interruptions | 13 | | | |
| participants with dose reductions | 4 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

5 years

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 20.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | All@Patients |
|-----------------------|--------------|

Reporting group description:

All@Patients

| | |
|-----------------------|------------------------|
| Reporting group title | Non Surg BGJ398@125 mg |
|-----------------------|------------------------|

Reporting group description:

Non Surg BGJ398@125 mg

| Serious adverse events | All@Patients | Non Surg BGJ398@125 mg | |
|---|-----------------|------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 9 / 26 (34.62%) | 9 / 26 (34.62%) | |
| number of deaths (all causes) | 3 | 3 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Investigations | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Surgical and medical procedures | | | |
| Cataract operation | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Ataxia | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epilepsy | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hemiparesis | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hydrocephalus | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neurological decompensation | | | |
| subjects affected / exposed | 2 / 26 (7.69%) | 2 / 26 (7.69%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 2 | |
| Neurological symptom | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Seizure | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperphosphataemia | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | All@Patients | Non Surg BGJ398@125 mg | |
|---|-------------------|---------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 26 / 26 (100.00%) | 26 / 26 (100.00%) | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 2 / 26 (7.69%) | 2 / 26 (7.69%) | |
| occurrences (all) | 4 | 4 | |
| Fatigue | | | |
| subjects affected / exposed | 9 / 26 (34.62%) | 9 / 26 (34.62%) | |
| occurrences (all) | 9 | 9 | |
| Gait disturbance | | | |
| subjects affected / exposed | 3 / 26 (11.54%) | 3 / 26 (11.54%) | |
| occurrences (all) | 3 | 3 | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 2 / 26 (7.69%) | 2 / 26 (7.69%) | |
| occurrences (all) | 5 | 5 | |
| Oedema peripheral | | | |

| | | | |
|---|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 3 / 26 (11.54%) 3 | 3 / 26 (11.54%) 3 | |
| Cyst subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | 1 / 26 (3.85%) 1 | |
| Pain subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | 1 / 26 (3.85%) 1 | |
| Reproductive system and breast disorders | | | |
| Bartholin's cyst subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 2 | 1 / 26 (3.85%) 2 | |
| Vaginal haemorrhage subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | 1 / 26 (3.85%) 1 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough subjects affected / exposed occurrences (all) | 2 / 26 (7.69%) 2 | 2 / 26 (7.69%) 2 | |
| Epistaxis subjects affected / exposed occurrences (all) | 2 / 26 (7.69%) 4 | 2 / 26 (7.69%) 4 | |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 2 / 26 (7.69%) 3 | 2 / 26 (7.69%) 3 | |
| Hiccups subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | 1 / 26 (3.85%) 1 | |
| Nasal inflammation subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | 1 / 26 (3.85%) 1 | |
| Sinus congestion subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | 1 / 26 (3.85%) 1 | |
| Psychiatric disorders | | | |

| | | | |
|--------------------------------------|-----------------|-----------------|--|
| Anxiety | | | |
| subjects affected / exposed | 2 / 26 (7.69%) | 2 / 26 (7.69%) | |
| occurrences (all) | 2 | 2 | |
| Confusional state | | | |
| subjects affected / exposed | 2 / 26 (7.69%) | 2 / 26 (7.69%) | |
| occurrences (all) | 2 | 2 | |
| Depression | | | |
| subjects affected / exposed | 2 / 26 (7.69%) | 2 / 26 (7.69%) | |
| occurrences (all) | 2 | 2 | |
| Insomnia | | | |
| subjects affected / exposed | 4 / 26 (15.38%) | 4 / 26 (15.38%) | |
| occurrences (all) | 4 | 4 | |
| Agitation | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences (all) | 1 | 1 | |
| Investigations | | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 2 / 26 (7.69%) | 2 / 26 (7.69%) | |
| occurrences (all) | 2 | 2 | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 3 / 26 (11.54%) | 3 / 26 (11.54%) | |
| occurrences (all) | 3 | 3 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 3 / 26 (11.54%) | 3 / 26 (11.54%) | |
| occurrences (all) | 4 | 4 | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 2 / 26 (7.69%) | 2 / 26 (7.69%) | |
| occurrences (all) | 2 | 2 | |
| Leukopenia | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences (all) | 3 | 3 | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences (all) | 1 | 1 | |
| Amylase increased | | | |

| | | | |
|---|---------------------------------|---------------------------------|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 26 (3.85%)</p> <p>1</p> | <p>1 / 26 (3.85%)</p> <p>1</p> | |
| <p>Blood bilirubin increased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 26 (3.85%)</p> <p>2</p> | <p>1 / 26 (3.85%)</p> <p>2</p> | |
| <p>Weight decreased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 26 (3.85%)</p> <p>1</p> | <p>1 / 26 (3.85%)</p> <p>1</p> | |
| <p>White blood cell count decreased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 26 (3.85%)</p> <p>1</p> | <p>1 / 26 (3.85%)</p> <p>1</p> | |
| <p>Injury, poisoning and procedural complications</p> <p>Fall</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 26 (7.69%)</p> <p>3</p> | <p>2 / 26 (7.69%)</p> <p>3</p> | |
| <p>Traumatic haematoma</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 26 (3.85%)</p> <p>1</p> | <p>1 / 26 (3.85%)</p> <p>1</p> | |
| <p>Cardiac disorders</p> <p>Palpitations</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 26 (3.85%)</p> <p>1</p> | <p>1 / 26 (3.85%)</p> <p>1</p> | |
| <p>Sinus bradycardia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 26 (3.85%)</p> <p>1</p> | <p>1 / 26 (3.85%)</p> <p>1</p> | |
| <p>Nervous system disorders</p> <p>Aphasia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 26 (11.54%)</p> <p>3</p> | <p>3 / 26 (11.54%)</p> <p>3</p> | |
| <p>Dizziness</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 26 (7.69%)</p> <p>2</p> | <p>2 / 26 (7.69%)</p> <p>2</p> | |
| <p>Headache</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>6 / 26 (23.08%)</p> <p>6</p> | <p>6 / 26 (23.08%)</p> <p>6</p> | |
| <p>Hemiparesis</p> | | | |

| | | |
|-----------------------------|-----------------|-----------------|
| subjects affected / exposed | 2 / 26 (7.69%) | 2 / 26 (7.69%) |
| occurrences (all) | 2 | 2 |
| Memory impairment | | |
| subjects affected / exposed | 2 / 26 (7.69%) | 2 / 26 (7.69%) |
| occurrences (all) | 2 | 2 |
| Seizure | | |
| subjects affected / exposed | 4 / 26 (15.38%) | 4 / 26 (15.38%) |
| occurrences (all) | 4 | 4 |
| Somnolence | | |
| subjects affected / exposed | 2 / 26 (7.69%) | 2 / 26 (7.69%) |
| occurrences (all) | 2 | 2 |
| Tremor | | |
| subjects affected / exposed | 2 / 26 (7.69%) | 2 / 26 (7.69%) |
| occurrences (all) | 2 | 2 |
| Anosmia | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Ataxia | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Cognitive disorder | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Dysaesthesia | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Dysgeusia | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Facial paresis | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Hemianopia | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Horner's syndrome | | |

| | | | |
|--------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences (all) | 1 | 1 | |
| Paraesthesia | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences (all) | 1 | 1 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 3 / 26 (11.54%) | 3 / 26 (11.54%) | |
| occurrences (all) | 3 | 3 | |
| Eye disorders | | | |
| Dry eye | | | |
| subjects affected / exposed | 3 / 26 (11.54%) | 3 / 26 (11.54%) | |
| occurrences (all) | 3 | 3 | |
| Eyelid ptosis | | | |
| subjects affected / exposed | 2 / 26 (7.69%) | 2 / 26 (7.69%) | |
| occurrences (all) | 2 | 2 | |
| Cataract | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences (all) | 2 | 2 | |
| Conjunctival hyperaemia | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences (all) | 1 | 1 | |
| Corneal infiltrates | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences (all) | 1 | 1 | |
| Eye irritation | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences (all) | 1 | 1 | |
| Keratopathy | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences (all) | 2 | 2 | |
| Ocular hyperaemia | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences (all) | 1 | 1 | |
| Gastrointestinal disorders | | | |

| | | |
|------------------------------|-----------------|-----------------|
| Constipation | | |
| subjects affected / exposed | 7 / 26 (26.92%) | 7 / 26 (26.92%) |
| occurrences (all) | 8 | 8 |
| Diarrhoea | | |
| subjects affected / exposed | 8 / 26 (30.77%) | 8 / 26 (30.77%) |
| occurrences (all) | 11 | 11 |
| Dyspepsia | | |
| subjects affected / exposed | 7 / 26 (26.92%) | 7 / 26 (26.92%) |
| occurrences (all) | 7 | 7 |
| Stomatitis | | |
| subjects affected / exposed | 5 / 26 (19.23%) | 5 / 26 (19.23%) |
| occurrences (all) | 10 | 10 |
| Aphthous ulcer | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Dry mouth | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Gastritis | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Gastrointestinal haemorrhage | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Glossodynia | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Haematochezia | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Haemorrhoids | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Lip dry | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |

| | | | |
|---|-----------------|-----------------|--|
| Lip pain | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences (all) | 1 | 1 | |
| Nausea | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences (all) | 1 | 1 | |
| Odynophagia | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences (all) | 1 | 1 | |
| Oral disorder | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences (all) | 1 | 1 | |
| Oral pain | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences (all) | 1 | 1 | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences (all) | 1 | 1 | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 4 / 26 (15.38%) | 4 / 26 (15.38%) | |
| occurrences (all) | 4 | 4 | |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 2 / 26 (7.69%) | 2 / 26 (7.69%) | |
| occurrences (all) | 2 | 2 | |
| Dry skin | | | |
| subjects affected / exposed | 4 / 26 (15.38%) | 4 / 26 (15.38%) | |
| occurrences (all) | 5 | 5 | |
| Nail disorder | | | |
| subjects affected / exposed | 2 / 26 (7.69%) | 2 / 26 (7.69%) | |
| occurrences (all) | 2 | 2 | |
| Onycholysis | | | |
| subjects affected / exposed | 3 / 26 (11.54%) | 3 / 26 (11.54%) | |
| occurrences (all) | 6 | 6 | |
| Palmar-plantar erythrodysaesthesia syndrome | | | |

| | | |
|-----------------------------|-----------------|-----------------|
| subjects affected / exposed | 3 / 26 (11.54%) | 3 / 26 (11.54%) |
| occurrences (all) | 4 | 4 |
| Skin ulcer | | |
| subjects affected / exposed | 2 / 26 (7.69%) | 2 / 26 (7.69%) |
| occurrences (all) | 2 | 2 |
| Blister | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Dermatitis bullous | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Erythema | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Hyperkeratosis | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 2 | 2 |
| Hypertrichosis | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Nail dystrophy | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Onychalgia | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 2 | 2 |
| Rash maculo-papular | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Skin disorder | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Skin exfoliation | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Skin irritation | | |

| | | | |
|---|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | 1 / 26 (3.85%) 1 | |
| Xeroderma subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | 1 / 26 (3.85%) 1 | |
| Renal and urinary disorders Urinary incontinence subjects affected / exposed occurrences (all) | 4 / 26 (15.38%) 4 | 4 / 26 (15.38%) 4 | |
| Chromaturia subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | 1 / 26 (3.85%) 1 | |
| Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | 1 / 26 (3.85%) 1 | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 2 / 26 (7.69%) 4 | 2 / 26 (7.69%) 4 | |
| Muscular weakness subjects affected / exposed occurrences (all) | 4 / 26 (15.38%) 6 | 4 / 26 (15.38%) 6 | |
| Musculoskeletal pain subjects affected / exposed occurrences (all) | 2 / 26 (7.69%) 2 | 2 / 26 (7.69%) 2 | |
| Myalgia subjects affected / exposed occurrences (all) | 2 / 26 (7.69%) 2 | 2 / 26 (7.69%) 2 | |
| Pain in extremity subjects affected / exposed occurrences (all) | 3 / 26 (11.54%) 4 | 3 / 26 (11.54%) 4 | |
| Infections and infestations Conjunctivitis subjects affected / exposed occurrences (all) | 2 / 26 (7.69%) 2 | 2 / 26 (7.69%) 2 | |

| | | |
|-----------------------------|----------------|----------------|
| Oral candidiasis | | |
| subjects affected / exposed | 2 / 26 (7.69%) | 2 / 26 (7.69%) |
| occurrences (all) | 2 | 2 |
| Folliculitis | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Fungal skin infection | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 2 | 2 |
| Herpes simplex | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Hordeolum | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Lip infection | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Nasopharyngitis | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Oral herpes | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Paronychia | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Pharyngitis | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Rash pustular | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |
| Rhinitis | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) |
| occurrences (all) | 1 | 1 |

| | | | |
|--|------------------------|------------------------|--|
| Vulvovaginal mycotic infection subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | 1 / 26 (3.85%) 1 | |
| Wound infection subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | 1 / 26 (3.85%) 1 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite subjects affected / exposed occurrences (all) | 4 / 26 (15.38%) 4 | 4 / 26 (15.38%) 4 | |
| Hyperglycaemia subjects affected / exposed occurrences (all) | 3 / 26 (11.54%) 5 | 3 / 26 (11.54%) 5 | |
| Hyperlipasaemia subjects affected / exposed occurrences (all) | 4 / 26 (15.38%) 5 | 4 / 26 (15.38%) 5 | |
| Hyperphosphataemia subjects affected / exposed occurrences (all) | 20 / 26 (76.92%) 43 | 20 / 26 (76.92%) 43 | |
| Hyponatraemia subjects affected / exposed occurrences (all) | 2 / 26 (7.69%) 4 | 2 / 26 (7.69%) 4 | |
| Hypophosphataemia subjects affected / exposed occurrences (all) | 4 / 26 (15.38%) 11 | 4 / 26 (15.38%) 11 | |
| Hypercalcaemia subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | 1 / 26 (3.85%) 1 | |
| Hypercreatininaemia subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 2 | 1 / 26 (3.85%) 2 | |
| Hyperkalaemia subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | 1 / 26 (3.85%) 1 | |
| Hypernatraemia | | | |

| | | | |
|-----------------------------|----------------|----------------|--|
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences (all) | 1 | 1 | |
| Hyperuricaemia | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences (all) | 1 | 1 | |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences (all) | 3 | 3 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | 1 / 26 (3.85%) | |
| occurrences (all) | 1 | 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|----------------|---|
| 01 August 2014 | exclusion criteria were updated to exclude patients with current evidence of corneal/keratopathy or retinal disorder, ophthalmologic eye exam assessments were added, patients with clinically significant hypokalemia were excluded |
| 01 April 2015 | Inclusion/Exclusion criteria were modified to exclude patients with FGFR1, 2, 3, and 4 amplifications and to include GBM and/or other glioma subtype patients with FGFR1-TACC1, FGFR3-TACC3 fusion and/or activating mutations in FGFR1, 2 or 3 gene. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

decision was made not to pursue further development for this disease indication. BGJ398 was out licensed and the indication was no longer pursued. Remaining patient continued treatment in post-trial settings.

Notes: