



Clinical trial results:

A multicenter medical safety follow-up study for patients with partial onset seizures who received more than 28 days of total exposure to BGG492 in studies BGG492A2207 and/or BGG492A2212

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2013-003431-29 |
| Trial protocol | IT |
| Global end of trial date | 21 September 2015 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 06 October 2016 |
| First version publication date | 06 October 2016 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | CBGG492A2216 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02150213 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Novartis Pharma AG |
| Sponsor organisation address | CH-4002, Basel, Switzerland, |
| Public contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, |
| Scientific contact | Clinical Disclosure Office, Novartis Pharma AG, 41 6133241111, |

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 | 21 September 2015 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 21 September 2015 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to observe if patients exposed to BGG492 for more than 28 days had developed uterine endometrial stromal sarcomas (females) and/or adrenal cortical adenomas (males and females) at least one year after treatment with BGG492 had been completed

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 | 28 August 2014 |
| 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 | Germany: 18 |
| Country: Number of subjects enrolled | Italy: 2 |
| Country: Number of subjects enrolled | Korea, Republic of: 17 |
| Country: Number of subjects enrolled | Hungary: 13 |
| Country: Number of subjects enrolled | Slovakia: 2 |
| Country: Number of subjects enrolled | United States: 7 |
| Worldwide total number of subjects | 59 |
| EEA total number of subjects | 35 |

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) | 56 |
| From 65 to 84 years | 3 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The purpose of this follow-up safety study was to provide medical follow-up to patients exposed to BGG492 for more than 28 days in Study BGG492A2207 and/or BGG492A2212.

Pre-assignment

Screening details:

The purpose of this follow-up safety study was to provide medical follow-up to patients exposed to BGG492 for more than 28 days in Study BGG492A2207 and/or BGG492A2212.

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 | BGG492 |
|-----------|--------|

Arm description:

This was a follow-up safety study where study treatment was not administered. Patients came from BGG492 studies where patients were previously exposed to > 28 days of BGG492 50 mg, 100 mg or 150 mg given orally three times a day

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | Selurampanel |
| Investigational medicinal product code | BGG492 |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Treatment was not administered in this study. Patients came from BGG492 studies where patients were previously exposed to > 28 days of BGG492 50 mg, 100 mg or 150 mg given orally three times a day

| Number of subjects in period 1 | BGG492 |
|--------------------------------|--------|
| Started | 59 |
| Completed | 57 |
| Not completed | 2 |
| Consent withdrawn by subject | 1 |
| Lost to follow-up | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------|
| Reporting group title | BGG492 |
|-----------------------|--------|

Reporting group description:

This was a follow-up safety study where study treatment was not administered. Patients came from BGG492 studies where patients were previously exposed to > 28 days of BGG492 50 mg, 100 mg or 150 mg given orally three times a day

| Reporting group values | BGG492 | Total | |
|---|---------|-------|--|
| Number of subjects | 59 | 59 | |
| 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) | 56 | 56 | |
| From 65-84 years | 3 | 3 | |
| 85 years and over | 0 | 0 | |
| Age Continuous | | | |
| Units: Years | | | |
| arithmetic mean | 43.2 | | |
| standard deviation | ± 11.58 | - | |
| Gender, Male/Female | | | |
| Units: Subjects | | | |
| Female | 31 | 31 | |
| Male | 28 | 28 | |

End points

End points reporting groups

| | |
|--|--------|
| Reporting group title | BGG492 |
| Reporting group description: This was a follow-up safety study where study treatment was not administered. Patients came from BGG492 studies where patients were previously exposed to > 28 days of BGG492 50 mg, 100 mg or 150 mg given orally three times a day | |

Primary: Incidence of adrenal cortical adenomas

| | |
|---|---|
| End point title | Incidence of adrenal cortical adenomas ^[1] |
| End point description: Incidence of adrenal cortical adenomas as assessed by non-contrast MRI of the abdomen (CT or ultrasound of the abdomen was permitted if MRI was contraindication). No statistical analysis was planned for this primary outcome | |
| End point type | Primary |
| End point timeframe: Minimum of one year after last dose of BGG492 in study BGG492A2207 or BGG492A2212 | |

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 statistical analysis was planned for this endpoint.

| End point values | BGG492 | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 59 | | | |
| Units: Participants | 3 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Incidence of uterine endometrial stromal sarcomas

| | |
|--|--|
| End point title | Incidence of uterine endometrial stromal sarcomas ^[2] |
| End point description: Incidence of uterine endometrial stromal sarcomas as assessed by sonogram/biopsy (females) No Statistical analysis was planned for this primary outcome. | |
| End point type | Primary |
| End point timeframe: Minimum of one year after last dose of BGG492 in study BGG492A2207 or BGG492A2212 | |

Notes:

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

Justification: No statistical analysis was planned for this endpoint.

| | | | | |
|-----------------------------|-----------------|--|--|--|
| End point values | BGG492 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 29 | | | |
| Units: Participants | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All Adverse events are reported in this record from First Patient First Treatment until Last Patient Last Visit.

Adverse event reporting additional description:

Occurrences causally related to treatment were assessed by investigator.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 18.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------|
| Reporting group title | BGG492 |
|-----------------------|--------|

Reporting group description:

This was a follow-up safety study where study treatment was not administered. Patients came from BGG492 studies where patients were previously exposed to > 28 days of BGG492 50 mg, 100 mg or 150 mg given orally three times a day

| Serious adverse events | BGG492 | | |
|---|----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 59 (8.47%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adrenal Adenoma | | | |
| alternative dictionary used: MedDRA 18.0 | | | |
| subjects affected / exposed | 3 / 59 (5.08%) | | |
| occurrences causally related to treatment / all | 2 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Angiomyolipoma | | | |
| alternative dictionary used: MedDRA 18.0 | | | |
| subjects affected / exposed | 1 / 59 (1.69%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reproductive system and breast disorders | | | |
| Ovarian cyst | | | |
| alternative dictionary used: MedDRA 18.0 | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 59 (1.69%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| | | | |
|---|----------------|--|--|
| Non-serious adverse events | BGG492 | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 3 / 59 (5.08%) | | |
| Renal and urinary disorders | | | |
| Renal Cyst | | | |
| alternative dictionary used: MedDRA 18.0 | | | |
| subjects affected / exposed | 3 / 59 (5.08%) | | |
| occurrences (all) | 3 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 18 December 2014 | <p>Where MRI was not appropriate for imaging of the adrenal gland, CT or, if CT was not available, ultrasound, were allowed as alternative procedures for imaging. Changes were made throughout the protocol to indicate that a "qualified specialist" could perform the sonogram, and not only gynecologists. Text was added to specify that if imaging of the adrenal gland had been performed outside of the study but at least 1 year after the last dose of BGG492, then it was not required to perform this assessment again in the context of this study, as long as the imaging report was available. Results from this imaging were recorded in the eCRF. Text was added above the Schedule of Assessments to emphasize that the assessments listed for Visits 3 and 5 were only required for patients who had findings on the adrenal and/or uterine imaging. The SAE reporting requirements specific to this study were clarified. The original protocol made reference to the use of MRI to collect density measurements in Hounsfield units. This was corrected throughout the protocol since density in Hounsfield units applies to CT scans.</p> |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported