



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
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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
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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
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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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.0
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Reporting groups

Reporting group title	BGG492
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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.</p> <p>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