Clinical trial results:
A single arm open label study to evaluate the pharmacodynamics and safety of a 4-week treatment with BI 144807 in patients with newly diagnosed wet age-related macular degeneration (wAMD).

Summary

EudraCT number	2013-004567-30
Trial protocol	HU DE AT
Global end of trial date	09 April 2015

Results information

Result version number	v1 (current)
This version publication date	23 April 2016
First version publication date	23 April 2016

Trial information

Trial identification

Sponsor protocol code	1313.20

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02121522
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Boehringer Ingelheim
Sponsor organisation address	Binger Strasse 173, Ingelheim am Rhein, Germany, 55216
Public contact	QRPE Processes and Systems Coordination Clinical Trial Information Disclosure, Boehringer Ingelheim, +1 8002430127, clintriage.rdg@boehringer-ingelheim.com
Scientific contact	QRPE Processes and Systems Coordination Clinical Trial Information Disclosure, Boehringer Ingelheim, +1 8002430127, clintriage.rdg@boehringer-ingelheim.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	26 August 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 March 2015
Global end of trial reached?	Yes
Global end of trial date	09 April 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of study 1313.20 was to investigate the effect of BI 144807 on central 1-mm retinal thickness (CRT) as assessed by spectral domain optical coherence tomography (SD-OCT) in patients with newly diagnosed wAMD.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were to be entered in the study. All subjects were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of all subjects was adhered to throughout the trial conduct.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 June 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	Austria: 8
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Hungary: 13
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	6
From 65 to 84 years	22

85 years and over	2

Subject disposition

Recruitment

Recruitment details:

This is a open-label, single-arm, 4-week proof-of-concept study.

Pre-assignment

Screening details:

All subjects were screened for eligibility to participate in trial. Subjects attended specialist sites to ensure that they (the subjects) met all implemented inclusion/exclusion criteria. Subjects were not to be randomised to trial drug if any of the specific entry criteria was violated. In this study,30 subjects enrolled and 14 subjects treated.

Period 1

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

Blinding implementation details:

This is a Non-randomised, not controlled and open-label study.

Arms

Arm title	BI 144807

Arm description:

Subjects were orally administered with 400 mg film coated tables twice daily (two tablets of 200 mg twice daily).

Arm type	Experimental
Investigational medicinal product name	BI 144807
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects were orally administered with BI 144807 400 mg film coated tables twice daily (two tablets of 200 mg twice daily).

Number of subjects in period 1[1]	BI 144807
Started	14
Completed	13
Not completed	1
Adverse event, non-fatal	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Baseline characteristics are based on the patients who were treated after successfully completing the screening period and received at least one dose of the trial medication.

Baseline characteristics

Reporting groups	
Reporting group title	BI 144807
Reporting group description:	
Subjects were orally administered with 400 mg film coated tables twice daily (two tablets of 200 mg twice daily).	

Reporting group values	BI 144807	Total	
Number of subjects	14	14	
Age categorical Units: Subjects			

Age Continuous			
Treated set (TS): All patients who were dispensed study medication and were documented to have taken at least one dose of study drug.			
Units: years			
arithmetic mean	75		
standard deviation	± 7.8	-	
Gender, Male/Female Units: participants			
Female	7	7	
Male	7	7	

End points

End points reporting groups

Reporting group title	BI 144807

Reporting group description:

Subjects were orally administered with 400 mg film coated tables twice daily (two tablets of 200 mg twice daily).

Primary: Change from baseline in CRT as measured by SD-OCT on day 29

End point title	Change from baseline in CRT as measured by SD-OCT on day 29[1]

End point description:

Change from baseline in central 1-mm retinal thickness (CRT) as measured by spectral domain optical coherence tomography (SD-OCT) on day 29.

Missing values are imputed by the worst observation carried forward (WOCF) measurement (including baseline).

End point type	Primary

End point timeframe:

Baseline (day 1) and day 29

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: This endpoint was evaluated only descriptively. Thus, no statistical hypothesis test were tested.

End point values	BI 144807			
Subject group type	Reporting group			
Number of subjects analysed	14[2]			
Units: µm				
arithmetic mean (standard deviation)	44 (± 151.5)			

Notes:

[2] - Treated set (WOCF)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in neovascular leakage area as assessed by FA on day 29

End point title	Change from baseline in neovascular leakage area as assessed by FA on day 29

End point description:

Change from baseline in neovascular leakage area as assessed by Fluorescein angiography (FA) on day 29. Baseline is defined as the last value collected before the first trial drug intake. Data collected after start of wet age-related macular degeneration (wAMD) therapy are set to missing.

Observed Case (OC): This method analysed only available data that were observed while patients were on treatment, ie., missing data were not imputed.

End point type	Secondary

End point timeframe:
Baseline and day 29

End point values	BI 144807			
Subject group type	Reporting group			
Number of subjects analysed	10[3]			
Units: mm²				
arithmetic mean (standard deviation)	-0.7 (± 1.4)			

Notes:
[3] - Treated set (OC)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From first drug administration until 5 days after last drug administration, up to 5 weeks.	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.0
Reporting groups	
Reporting group title	BI 144807
Reporting group description: Subjects were orally administered with 400 mg film coated tables twice daily (two tablets of 200 mg twice daily).	

Serious adverse events	BI 144807		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 14 (7.14%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Eye disorders			
Retinal haemorrhage			
subjects affected / exposed	1 / 14 (7.14%)		
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	BI 144807		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 14 (42.86%)		
Investigations			
Body temperature increased			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		

Nervous system disorders Headache subjects affected / exposed occurrences (all)	 2 / 14 (14.29%) 2		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	 1 / 14 (7.14%) 1		
Eye disorders Retinal haemorrhage subjects affected / exposed occurrences (all)	 1 / 14 (7.14%) 1		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all)	 1 / 14 (7.14%) 1 1 / 14 (7.14%) 1		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	 1 / 14 (7.14%) 1		
Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Oral herpes subjects affected / exposed occurrences (all)	 1 / 14 (7.14%) 1 1 / 14 (7.14%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 June 2014	By Amendment 1 the assessment of lesion size by FA over time (absolute and as change from baseline) was added as further efficacy endpoint. Further, it was clarified that cancers of newhistology or exacerbation of an existing cancer were always considered an SAE. Inhaled corticosteroids were not permitted as concomitant therapy. It was clarified that informed consent for PK evaluations of the eye could be obtained after Visit 1 but prior to aqueous humour sampling and that the last PK sample for plasma evaluation was to be taken at Visit 7. Moreover, it was specified that myopia of more than 8 diopters in the study eye is an exclusion criterion also if corrected by laser operation (Exclusion Criterion 1) and it was clarified that cardiac conditions as exclusion criterion also include tachycardia (Exclusion Criterion 16). In addition, the wording "known allergy to fluorescein sodium for injection" in Exclusion Criterion 6 was changed to "known allergy or contra-indication to contrast agents employed in study". It was added that before Visit 6 the administration times of the preceding two days are to be recorded. In the section on the definition of AESIs (Section 9.5.3.2.1), QTc was precisely defined as QTcF prolongation. It was added that thyroid stimulating hormone (TSH) was measured at the screening visit. It was detailed that in addition to the AE reports of the investigator, quantitative ECG data and qualitative findings in ECGs will be transferred from the VRC and analysed; the VCR will also provide indicators for the readability of the ECGs. Quantitative and qualitative ECG data from the ECG reading centre were reported descriptively.

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.

The trial was prematurely discontinued as the preliminary data showed that the likelihood to meet the trial's primary efficacy endpoint would have been low even if the patient recruitment had been continued.

Notes: