



Clinical trial results:

A Phase IIA, Open-Label, Single-Arm, Two Stage, Multi-Centre Study to Investigate the Pharmacodynamics, Pharmacokinetics, Safety and Tolerability of Repeated Subcutaneous Administration of BIM23B065 in Subjects with Acromegaly

Summary

EudraCT number	2015-003868-37
Trial protocol	HU BE BG
Global end of trial date	26 May 2017

Results information

Result version number	v1 (current)
This version publication date	03 August 2018
First version publication date	03 August 2018

Trial information

Trial identification

Sponsor protocol code	D-FR-10380-002
-----------------------	----------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03045302
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ipsen Pharma SAS
Sponsor organisation address	65, quai Georges Gorse, Boulogne-Billancourt, France, 92100
Public contact	Medical Director, Ipsen Pharma SAS, clinical.trials@ipsen.com
Scientific contact	Medical Director, Ipsen Pharma SAS, clinical.trials@ipsen.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 May 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 May 2017
Global end of trial reached?	Yes
Global end of trial date	26 May 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the pharmacodynamics (PD) of repeated administration of BIM23B065 in reducing growth hormone (GH) in subjects with acromegaly.

Protection of trial subjects:

The study was conducted under the provision of the Declaration of Helsinki, in accordance with the International Council for Harmonisation Consolidated Guideline on Good Clinical Practice and in compliance with Independent Ethic Committees/Independent Review Boards and informed consent regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 January 2017
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	Hungary: 2
Country: Number of subjects enrolled	Ukraine: 2
Worldwide total number of subjects	4
EEA total number of subjects	2

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)	3
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects with acromegaly were recruited from 26 January 2017 in 4 study centres in 4 countries. Stage 1 of the study consisted of a twice daily (BID) regimen of BIM23B065, and a Stage 2 with a three times daily regimen of BIM23B065 was planned but not conducted due to early termination of the study on 26 May 2017.

Pre-assignment

Screening details:

7 subjects were screened and 3 failed screening (1 subject did not meet eligibility criteria and 2 subjects did not complete screening procedures due to the early study termination).

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	BIM23B065 BID Stage 1
------------------	-----------------------

Arm description:

Subjects received twice daily administrations of BIM23B065 (at an interval of 12 +/- 1 hour) as subcutaneous injections in the abdominal region during the Stage 1 treatment period which consisted of a titration phase and a treatment phase.

Titration phase (Days 1 to 6): Subjects received BIM23B065 0.4 milligram (mg) BID (Days 1 and 2), then BIM23B065 0.6 mg BID (Days 3 and 4) and BIM23B065 0.8 mg BID (Days 5 and 6).

Treatment phase (Days 7 to 14): Following titration, a stable target dose of BIM23B065 1.0 mg BID was planned to be administered from Day 7 to Day 14.

Arm type	Experimental
Investigational medicinal product name	BIM23B065
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received subcutaneous injections BID in the abdominal region administered by a healthcare professional. During the treatment period the possible doses of BIM23B065 (1.0 mg/millilitre [mL]) were: 0.4 mg, 0.6 mg, 0.8 mg up to a target dose of 1.0 mg BID administered as volumes of 0.4 mL, 0.6 mL, 0.8 mL or 1.0 mL respectively.

Number of subjects in period 1	BIM23B065 BID Stage 1
Started	4
Completed	3
Not completed	1
Pre-treatment adverse event	1

Baseline characteristics

Reporting groups

Reporting group title	BIM23B065 BID Stage 1
-----------------------	-----------------------

Reporting group description:

Subjects received twice daily administrations of BIM23B065 (at an interval of 12 +/- 1 hour) as subcutaneous injections in the abdominal region during the Stage 1 treatment period which consisted of a titration phase and a treatment phase.

Titration phase (Days 1 to 6): Subjects received BIM23B065 0.4 milligram (mg) BID (Days 1 and 2), then BIM23B065 0.6 mg BID (Days 3 and 4) and BIM23B065 0.8 mg BID (Days 5 and 6).

Treatment phase (Days 7 to 14): Following titration, a stable target dose of BIM23B065 1.0 mg BID was planned to be administered from Day 7 to Day 14.

Reporting group values	BIM23B065 BID Stage 1	Total	
Number of subjects	4	4	
Age categorical			
Units: Subjects			

Age continuous			
Units: Years			
arithmetic mean	53.0		
standard deviation	± 15.12	-	
Gender categorical			
Units: Subjects			
Female	4	4	
Male	0	0	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Black or African American	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
White	4	4	
Unknown or Not Reported	0	0	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	4	4	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	BIM23B065 BID Stage 1
Reporting group description:	
Subjects received twice daily administrations of BIM23B065 (at an interval of 12 +/- 1 hour) as subcutaneous injections in the abdominal region during the Stage 1 treatment period which consisted of a titration phase and a treatment phase.	
Titration phase (Days 1 to 6): Subjects received BIM23B065 0.4 milligram (mg) BID (Days 1 and 2), then BIM23B065 0.6 mg BID (Days 3 and 4) and BIM23B065 0.8 mg BID (Days 5 and 6).	
Treatment phase (Days 7 to 14): Following titration, a stable target dose of BIM23B065 1.0 mg BID was planned to be administered from Day 7 to Day 14.	

Primary: The number of subjects who were GH Responders at Day 14 of the Treatment Period

End point title	The number of subjects who were GH Responders at Day 14 of the Treatment Period ^[1]
-----------------	--

End point description:

A GH responder was defined as a subject with mean serum GH concentration ≤ 2.5 micrograms per litre (mcg/L) or $>50\%$ reduction from mean baseline GH concentration after a 6-day titration and an 8-day treatment period with BIM23B065. The mean serum concentration of GH was measured over 6 hours at baseline (Day -1) and on Day 14. The number of subjects who were GH responders at Day 14 of the treatment period is presented.

The Efficacy Evaluable population consisted of all subjects with at least 1 BIM23B065 administration with available PD data and no protocol deviations with relevant impact on PD data, who had an evaluable primary efficacy endpoint (mean concentration of GH over 6 hours) at baseline and at Day 14.

End point type	Primary
----------------	---------

End point timeframe:

From baseline (Day -1) to Day 14.

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: Data is reported for Stage 1 of the study which was a single reporting group stage and therefore comparative statistical analyses between groups is not applicable.

End point values	BIM23B065 BID Stage 1			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Subjects	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment emergent adverse events were collected from Day 1 of the treatment period up to the end of the study (up to 4 months).

Adverse event reporting additional description:

The Safety population consisted of all subjects with at least 1 BIM23B065 administration.

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

Dictionary used

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

Dictionary version	20.0
--------------------	------

Reporting groups

Reporting group title	BIM23B065 BID Stage 1
-----------------------	-----------------------

Reporting group description:

Subjects received twice daily administrations of BIM23B065 (at an interval of 12 +/- 1 hour) as subcutaneous injections in the abdominal region during the Stage 1 treatment period which consisted of a titration phase and a treatment phase.

Titration phase (Days 1 to 6): Subjects received BIM23B065 0.4 mg BID (Days 1 and 2), then BIM23B065 0.6 mg BID (Days 3 and 4) and BIM23B065 0.8 mg BID (Days 5 and 6).

Treatment phase (Days 7 to 14): Following titration, a stable target dose of BIM23B065 1.0 mg BID was planned to be administered from Day 7 to Day 14.

Serious adverse events	BIM23B065 BID Stage 1		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	BIM23B065 BID Stage 1		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 4 (50.00%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Cardiac disorders			
Bradycardia			

subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 2		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1 1 / 4 (25.00%) 1		
Hepatobiliary disorders Cholelithiasis subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 September 2016	- An additional exclusion criterion was added, to exclude subjects with unsubstituted/untreated hypoadrenalism. - Serum cortisol was added as a safety endocrine parameter. - The total blood volume was amended in the Blood Sampling Summary. - The Global Patient Safety contact details were amended.

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 sponsor stopped the study early as the preliminary results in 3 subjects dosed with BIM23B065 showed an inadequate PD profile and efficacy. The enrolled subjects only received BID treatment. Only the primary endpoint results are reported.

Notes: