Clinical trial results:
An open-label, single arm, Phase III study to assess the self-administration of AOP2014 using a pre-filled pen, developed for the treatment of Polycythemia Vera patients

Summary

EudraCT number	2014-001356-31
Trial protocol	HU SK AT CZ BG PL
Global end of trial date	21 December 2015

Results information

Result version number	v1 (current)
This version publication date	11 March 2018
First version publication date	11 March 2018

Trial information

Trial identification

Sponsor protocol code	PEN-PV

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AOP Orphan Pharmaceuticals AG
Sponsor organisation address	Wilhelminenstrasse 91/II f/B4, Vienna, Austria, 1160
Public contact	Head of Clinical Operations, AOP Orphan Pharmaceuticals AG, +43 15037244 46, michael.zoerer@aoporphan.com
Scientific contact	Head of Clinical Operations, AOP Orphan Pharmaceuticals AG, +43 15037244 46, michael.zoerer@aoporphan.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	19 January 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 December 2015
Global end of trial reached?	Yes
Global end of trial date	21 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the ease of AOP2014 self-administration using dedicated questionnaires.

Protection of trial subjects:

An independent DMC was established that reviewed accumulated data on safety as well as efficacy in an open-label manner in regular intervals. Following the meetings the DMC advised the sponsor in writing on outcomes and findings of the meeting. Per the signed DMC charter the DMC took responsibility for continued safety as well as efficacy oversight.

Background therapy:

Low dose aspirin (acetylsalicylic acid) (100 mg/day) administered to all patients for the duration of study treatment, unless contraindicated.

Evidence for comparator: -

Actual start date of recruitment	24 June 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 4
Country: Number of subjects enrolled	Slovakia: 1
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Bulgaria: 10
Country: Number of subjects enrolled	Czech Republic: 5
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Hungary: 5
Country: Number of subjects enrolled	Ukraine: 6
Worldwide total number of subjects	36
EEA total number of subjects	30

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	24
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

From patients who had completed the AOP2014 arm of the PROUD-PV study or were participating in the CONTINUATION-PV study, 36 subjects were chosen according to the inclusion and exclusion criteria.

Period 1

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

Arms

Arm title	AOP2014 administration via pen

Arm description:

AOP2014 self-administered via a pre-filled pen at the individualized dose which delivers the optimal disease response.

Arm type	Experimental
Investigational medicinal product name	AOP2014
Investigational medicinal product code	AOP2014
Other name	Pegylated Proline-Interferon α-2b
Pharmaceutical forms	Solution for injection/infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

AOP2014 was self-administered using a pre-filled pen every 14 days at the individualized dose delivering the optimal disease response (Haematocrit<45%, Platelets <400 x 109/L and White blood cells <10 x 109/L), as determined previously during the PROUD-PV Study and maintained for the CONTINUATION-PV Study.

Number of subjects in period 1	AOP2014 administration via pen
Started	36
Completed	36

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	36	36	
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)	24	24	
From 65-84 years	12	12	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	58.5		
standard deviation	± 9.99	-	
Gender categorical Units: Subjects			
Female	13	13	
Male	23	23	
Duration of AOP treatment at the start of the study Units: months			
arithmetic mean	15.65		
standard deviation	± 2.596	-	

End points

End points reporting groups

Reporting group title	AOP2014 administration via pen

Reporting group description:

AOP2014 self-administered via a pre-filled pen at the individualized dose which delivers the optimal disease response.

Primary: Evaluation of ease of self-administration based on questionnaire A and B

End point title	Evaluation of ease of self-administration based on questionnaire A and B[1]

End point description:

Full success was declared if questions "Experience any technical problems with the pen during the injection?" and "Withdraw the pen before the injection was complete, as evidenced by the supervising Investigator?") where answered 'No'.

End point type	Primary

End point timeframe:

Evaluated according to questionnaire answered by investigators at visits with supervised study treatment self-administration.

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: Only descriptive statistics were planned.

End point values	AOP2014 administration via pen			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: subjects				
Visit 1 - Full success	29			
Visit 2 - Full success	33			
Visit 7 - Fullsuccess	36			

Statistical analyses

No statistical analyses for this end point

Primary: Failure rate - Questionnaire A

End point title	Failure rate - Questionnaire A[2]

End point description:

Failure rate (%) is calculated as (actual score/highest score)*100.

End point type	Primary

End point timeframe:

Evaluated according to questionnaire answered by investigators at visits with supervised study treatment self-administration.

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: Only descriptive statistics were planned to evaluate if objective defined below was met.
• To achieve < 34.0% failure rate at supervised self-administration 1 (Visit 1) for both questionnaires
• To achieve <17.0% failure rate at supervised self-administration 2 (Visit 2) for both questionnaires
• Failure rate < 50.0% for each questionnaire at all subsequent visits

End point values	AOP2014 administration via pen			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: percent				
arithmetic mean (standard deviation)				
Visit 1	13.1 (± 15.788)			
Visit 2	5.95 (± 12.489)			
Visit 7	0 (± 0)			

Statistical analyses

No statistical analyses for this end point

Primary: Failure rate - Questionnaire B

End point title	Failure rate - Questionnaire B[3]

End point description:

Failure rate (%) is calculated as (actual score/highest score)*100.

End point type	Primary

End point timeframe:

Evaluated according to questionnaire answered by patient at each study treatment self-administration.

Notes:

[3] - 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: Only descriptive statistics were planned to evaluate if objective defined below was met.
• To achieve < 34.0% failure rate at supervised self-administration 1 (Visit 1) for both questionnaires
• To achieve <17.0% failure rate at supervised self-administration 2 (Visit 2) for both questionnaires
• Failure rate < 50.0% for each questionnaire at all subsequent visits

End point values	AOP2014 administration via pen			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: percent				
arithmetic mean (standard deviation)				
Visit 1	6.94 (± 13.437)			
Visit 2	0.46 (± 2.778)			
Visit 3	0.93 (± 3.872)			
Visit 4	0 (± 0)			
Visit 5	0.46 (± 2.778)			
Visit 6	0 (± 0)			

Visit 7	0 (± 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of responders by visit

End point title	Number of responders by visit

End point description:

Disease response (haematological response with spleen normality) was defined as:
- Haematocrit < 45% without phlebotomy (at least 3 months since the last phlebotomy).
- Platelets < 400 x 109/L.
- White blood cells < 10 x 109/L.
- Normal spleen size.

End point type	Secondary

End point timeframe:

Disease response rate evaluated at first (visit 1) and last (visit 7) study visit.

End point values	AOP2014 administration via pen			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: subjects				
Visit 1	15			
Visit 7	17			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of haematological responders by visit

End point title	Number of haematological responders by visit

End point description:

Disease response (haematological response) was defined as:
- Haematocrit < 45% without phlebotomy (at least 3 months since the last phlebotomy).
- Platelets < 400 x 109/L.
- White blood cells < 10 x 109/L.

End point type	Secondary

End point timeframe:

Disease response rate (without spleen size) evaluated at first (visit 1) and last (visit 7) study visit.

End point values	AOP2014 administration via pen			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: subjects				
Visit 1	26			
Visit 7	27			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
All adverse events occurring during the course of the clinical study were collected.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups	
Reporting group title	Overall trial
Reporting group description:	
Treatment emergent adverse events that started in PEN-PV.	

Serious adverse events	Overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 36 (2.78%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 36 (38.89%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Aspartate aminotransferase			

increased			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Hepatic enzyme increased			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	3		
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	4 / 36 (11.11%)		
occurrences (all)	4		
Thrombocytopenia			
subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	4		
Anaemia			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
General disorders and administration site conditions			
Facial pain			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	2		
Chest pain			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	1		
Diarrhoea			

subjects affected / exposed occurrences (all) Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Rectal fissure subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 2 1 / 36 (2.78%) 1 1 / 36 (2.78%) 1 1 / 36 (2.78%) 1		
Reproductive system and breast disorders Erectile dysfunction subjects affected / exposed occurrences (all)	 1 / 36 (2.78%) 1		
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all) Rhinitis atrophic subjects affected / exposed occurrences (all)	 1 / 36 (2.78%) 1 1 / 36 (2.78%) 2		
Skin and subcutaneous tissue disorders Erythrosis subjects affected / exposed occurrences (all)	 1 / 36 (2.78%) 1		
Psychiatric disorders Affective disorder subjects affected / exposed occurrences (all) Anxiety subjects affected / exposed occurrences (all) Mood swings subjects affected / exposed occurrences (all)	 1 / 36 (2.78%) 1 1 / 36 (2.78%) 1 1 / 36 (2.78%) 1		

Nervousness subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1		
Renal and urinary disorders Calculus urinary subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1		
Musculoskeletal and connective tissue disorders Pain in extremity subjects affected / exposed occurrences (all) Temporomandibular joint syndrome subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 2 1 / 36 (2.78%) 1		
Infections and infestations Acute sinusitis subjects affected / exposed occurrences (all) Cystitis subjects affected / exposed occurrences (all) Bronchitis subjects affected / exposed occurrences (all) Infection subjects affected / exposed occurrences (all) Rhinitis subjects affected / exposed occurrences (all) Viraemia subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 2 1 / 36 (2.78%) 1 1 / 36 (2.78%) 1 1 / 36 (2.78%) 1 1 / 36 (2.78%) 1 1 / 36 (2.78%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported