Clinical trial results:
Efficacy of Endothelin 1 receptor antagonist Bosentan in secondary Raynauds Syndrom

Summary

EudraCT number	2004-002686-21
Trial protocol	AT
Global end of trial date	29 December 2009

Results information

Result version number	v1 (current)
This version publication date	01 March 2022
First version publication date	01 March 2022

Trial information

Trial identification

Sponsor protocol code	Bosentan1

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medical University
Sponsor organisation address	Anichstrasse 35, Innsbruck, Austria, 6020
Public contact	Wolfram Jaschke Consultant, Department of Dermatology, Venereology and Allergy Medical University Innsbruck, +43 51250483671, wolfram.jaschke@i-med.ac.at
Scientific contact	Wolfram Jaschke Consultant, Department of Dermatology, Venereology and Allergy Medical University Innsbruck, +43 51250483671, wolfram.jaschke@i-med.ac.at

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	29 December 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 December 2009
Global end of trial reached?	Yes
Global end of trial date	29 December 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Efficacy of bosentan in secondary raynauds syndrome.

Protection of trial subjects:

Patients were excluded if they had primary RP (Raynaud’s phenomenon) or RP not associated with SSc (systemic sclerosis), active digital ulcer or gangrene, abnormal haemostasis, platelet alterations and evidence of uncontrolled cardiovascular, pulmonary, hepatic or renal disease. Other exclusion criteria were treatment with prostanoids within 3 months of enrolment, previous use of bosentan or other ET receptor blockers, phosphodiesterase-V-inhibitors and any medication contraindicating the administration of bosentan. Vasodilator drugs for arterial hypertension and the use of hand warmers or electric gloves were allowed, whereas topical treatment with glyceryl nitrate and therapy with paraffin wax hand baths were discontinued 4 weeks before starting the study. Women of child-bearing potential were required to have a negative pregnancy test before study initiation and apply effective contraceptive methods. All subjects were informed about the nature and aim of the study, and gave their informed written consent to participate.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 February 2005
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: 17
Worldwide total number of subjects	17
EEA total number of subjects	17

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)	14
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was designed as a prospective, randomized, single-centre, observer-blinded, placebo-controlled trial and was conducted over the cold winter months to maximize the development of RP (Raynaud’s phenomenon) as well as to minimize the seasonal effects on RP.

Period 1

Period 1 title	Pre-treatment (2 weeks)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Selection
Arm description:	
Randomization of trial participants	
Arm type	Selection
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Selection
Started	17
Completed	17

Period 2

Period 2 title	Treatment (16 weeks)
Is this the baseline period?	Yes[1]
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes

Arm title	Bosentan
Arm description:	
62.5mg bosentan twice daily for 4 weeks, followed by 125mg twice daily for 12 weeks	
Arm type	Experimental
Investigational medicinal product name	Bosentan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details:	
62.5mg bosentan twice daily for 4 weeks, followed by 125mg twice daily for 12 weeks	

Arm title	Placebo
Arm description:	
Placebo	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details:	
62.5mg placebo twice daily for 4 weeks, followed by 125mg twice daily for 12 weeks	

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: In the pre-treatment period subjects were randomized to one of the arms.

Number of subjects in period 2	Bosentan	Placebo
Started	9	8
Completed	8	8
Not completed	1	0
Adverse event, non-fatal	1	-

Period 3

Period 3 title	Post-treatment follow-up (8 weeks)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Follow-up
Arm description:	
Follow-up visits were conducted for the trial participants.	
Arm type	Follow-up
No investigational medicinal product assigned in this arm	

Number of subjects in period 3	Follow-up
Started	16
Completed	16

Baseline characteristics

Reporting groups	
Reporting group title	Bosentan
Reporting group description:	
62.5mg bosentan twice daily for 4 weeks, followed by 125mg twice daily for 12 weeks	
Reporting group title	Placebo
Reporting group description:	
Placebo	

Reporting group values	Bosentan	Placebo	Total
Number of subjects	9	8	17
Age categorical Units: Subjects			
Adults (18-64 years)	9	8	17
From 65-84 years	0	0	0
Age continuous Units: years			
median	43	63.5	
standard deviation	± 11.2	± 9.9	-
Gender categorical Units: Subjects			
Female	9	8	17
Male	0	0	0

End points

End points reporting groups

Reporting group title	Selection
Reporting group description:	
Randomization of trial participants	
Reporting group title	Bosentan
Reporting group description:	
62.5mg bosentan twice daily for 4 weeks, followed by 125mg twice daily for 12 weeks	
Reporting group title	Placebo
Reporting group description:	
Placebo	
Reporting group title	Follow-up
Reporting group description:	
Follow-up visits were conducted for the trial participants.	

Primary: Primary Endpoint

End point title	Primary Endpoint[1]
End point description:	
The primary outcome was the change in severity of RP attacks, measured by the Raynaud condition score (RCS), and its related variables frequency, duration and pain at the end of the treatment period at Week 16 compared with the baseline.	
End point type	Primary
End point timeframe:	
Day 1 to Week 16	

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: Statistical analysis was done within groups.

End point values	Bosentan	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	8		
Units: RCS Score				
median (confidence interval 95%)	-36 (-75 to 4)	-31 (-66 to 4)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Day 0 to week 16	
Assessment type	Systematic
Dictionary used	
Dictionary name	CTCAE
Dictionary version	3.0
Reporting groups	
Reporting group title	Bosentan
Reporting group description: 62.5mg bosentan twice daily for 4 weeks, followed by 125mg twice daily for 12 weeks	
Reporting group title	Placebo
Reporting group description: Placebo	

Serious adverse events	Bosentan	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Bosentan	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	
Skin and subcutaneous tissue disorders			
treatment-related peripheral oedema			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	
occurrences (all)	1	0	

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/20040526