Clinical trial results:
A multicentre, open-label study of propranolol in infants with proliferating infantile hemangioma requiring systemic therapy

Summary

EudraCT number	2010-023488-16
Trial protocol	FR
Global end of trial date	12 December 2013

Results information

Result version number	v1 (current)
This version publication date	17 February 2016
First version publication date	17 February 2016

Trial information

Trial identification

Sponsor protocol code	V00400SB301

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Pierre Fabre Dermatologie
Sponsor organisation address	45, Place Abel Gance, Boulogne, France, 92100
Public contact	Medical and/or Clinical Study Manager, Pierre Fabre Dermatologie, contact_essais_cliniques@pierre-fabre.com
Scientific contact	Medical and/or Clinical Study Manager, Pierre Fabre Dermatologie, contact_essais_cliniques@pierre-fabre.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	12 June 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 December 2013
Global end of trial reached?	Yes
Global end of trial date	12 December 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objectives of this study are to allow the use of propranolol with adequate conditions of administration and follow up in infants still requiring this systemic treatment (in the Investigator's opinion) after their participation to a previous trials. As requested in such conditions, the safety profile (included any potential long-term post-treatment impact) and the effect on the resolution of IH are documented.

Protection of trial subjects:

Clinical (including respiratory rate and vital sign measurements) and paraclinical (lab tests (haematology, biochemistry, glycemia (pin-prick) and ECG) examinations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 April 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	17 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 11
Worldwide total number of subjects	11
EEA total number of subjects	11

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)	11
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

French patients who has received study treatment in a previous studies and completed the corresponding end of study visit within the previous 6 months, and who has still required this systemic therapy in the investigator's opinion.

Period 1

Period 1 title	24-week study treatment period
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Propranolol 2 mg/kg/day - 24 weeks

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Propranolol hydrochloride oral solution
Investigational medicinal product code	V0400SB
Other name	Hemangiol
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

D0: 1 mg/kg/day
D7: increase to 2 mg/kg/day
during 24 weeks

Arm title	Propranolol 3 mg/kg/day - 24 weeks

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Propranolol hydrochloride oral solution
Investigational medicinal product code	V0400SB
Other name	Hemangiol
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

D0: 1 mg/kg/day
D7: increase to 2 mg/kg/day
D14: increase to 3 mg/kg/day
during 24 weeks.

Number of subjects in period 1	Propranolol 2 mg/kg/day - 24 weeks	Propranolol 3 mg/kg/day - 24 weeks
Started	4	7
Completed	4	1
Not completed	0	6
Treatment unit	-	1
'treatment effect/Improvement '	-	5

Period 2	
Period 2 title	72-week follow-up period (no study drug)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	72-week Follow-up period of 2 or 3mg/kg/day
Arm description: -	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	72-week Follow-up period of 2 or 3mg/kg/day
Started	5
Completed	10
Not completed	1
Lost to follow-up	1
Joined	6
Prematurely discontiued the treatment period	6

Baseline characteristics

Reporting groups

Reporting group title	24-week study treatment period

Reporting group description: -

Reporting group values	24-week study treatment period	Total	
Number of subjects	11	11	
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	11	11	
Age continuous Units: days			
arithmetic mean	196		
full range (min-max)	101 to 397	-	
Gender categorical Units: Subjects			
Female	10	10	
Male	1	1	

Subject analysis sets

Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis

Subject analysis set description:

All included and treated patients.

Reporting group values	Full analysis set		
Number of subjects	11		
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	11		
Age continuous Units: days			
arithmetic mean	196		
full range (min-max)	101 to 397		
Gender categorical Units: Subjects			
Female	10		
Male	1		

End points

End points reporting groups

Reporting group title	Propranolol 2 mg/kg/day - 24 weeks
Reporting group description: -	
Reporting group title	Propranolol 3 mg/kg/day - 24 weeks
Reporting group description: -	
Reporting group title	72-week Follow-up period of 2 or 3mg/kg/day
Reporting group description: -	
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis
Subject analysis set description:	
All included and treated patients.	

Primary: IH improvement

End point title	IH improvement[1]
End point description:	
End point type	Primary
End point timeframe:	
at each planned visit (11 visits)	

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: As a consequence of the low number of included patients (11 patients), no descriptive statistics were performed , only individual tabulated listings were provided.

End point values	Full analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: subject				
number (not applicable)	11			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Whole study period	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups	
Reporting group title	Study treatment period
Reporting group description: All treated subjects	
Reporting group title	Long term follow-up period
Reporting group description: -	

Serious adverse events	Study treatment period	Long term follow-up period	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Study treatment period	Long term follow-up period	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 11 (100.00%)	11 / 11 (100.00%)	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 11 (18.18%)	2 / 11 (18.18%)	
occurrences (all)	2	2	
Ear and labyrinth disorders			

External ear inflammation			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Conjunctivitis			
subjects affected / exposed	1 / 11 (9.09%)	1 / 11 (9.09%)	
occurrences (all)	1	2	
Gastrointestinal disorders			
Toothache			
subjects affected / exposed	3 / 11 (27.27%)	0 / 11 (0.00%)	
occurrences (all)	4	0	
Diarrhoea			
subjects affected / exposed	2 / 11 (18.18%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
vomiting			
subjects affected / exposed	2 / 11 (18.18%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Asthma			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Psychiatric disorders			
Middle insomnia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 11 (45.45%)	5 / 11 (45.45%)	
occurrences (all)	6	13	
Bronchiolitis			
subjects affected / exposed	3 / 11 (27.27%)	1 / 11 (9.09%)	
occurrences (all)	3	1	
Bronchitis			

subjects affected / exposed	3 / 11 (27.27%)	2 / 11 (18.18%)	
occurrences (all)	5	3	
Gastroenteritis			
subjects affected / exposed	3 / 11 (27.27%)	3 / 11 (27.27%)	
occurrences (all)	5	3	
Otitis media			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	1 / 11 (9.09%)	1 / 11 (9.09%)	
occurrences (all)	1	2	
Varicella			
subjects affected / exposed	1 / 11 (9.09%)	2 / 11 (18.18%)	
occurrences (all)	1	2	
Viral infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Ear infection			
subjects affected / exposed	0 / 11 (0.00%)	2 / 11 (18.18%)	
occurrences (all)	0	3	
Laryngitis			
subjects affected / exposed	0 / 11 (0.00%)	2 / 11 (18.18%)	
occurrences (all)	0	2	
Folliculitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Tonsillitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Tracheitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 October 2011	- Removal of one visit (no particular safety issue was expected at this visit), - Removal for need to collect blood in fasting state for screening laboratory tests, - change in the sponsor's contact for notification of SAEs, - change in the sponsor's personnel list.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported