



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 | Hemangirol |
| 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 | Hemangirol |
| 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 discontinued 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 full range (min-max) | 196 101 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 full range (min-max) | 196 101 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 occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 11 (0.00%) 0 | |
| Eye disorders Conjunctivitis subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 1 / 11 (9.09%) 2 | |
| Gastrointestinal disorders Toothache subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) vomiting subjects affected / exposed occurrences (all) | 3 / 11 (27.27%) 4 2 / 11 (18.18%) 2 2 / 11 (18.18%) 2 | 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Asthma subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 0 / 11 (0.00%) 0 | 0 / 11 (0.00%) 0 1 / 11 (9.09%) 1 | |
| Psychiatric disorders Middle insomnia subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 11 (0.00%) 0 | |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Bronchiolitis subjects affected / exposed occurrences (all) Bronchitis | 5 / 11 (45.45%) 6 3 / 11 (27.27%) 3 | 5 / 11 (45.45%) 13 1 / 11 (9.09%) 1 | |

| | | | |
|------------------------------------|-----------------|-----------------|--|
| 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 | <ul style="list-style-type: none">- 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