



## Clinical trial results:

**Therapeutic effect of propranolol in a series of patients with von Hippel-Lindau disease and retinal hemangioblastomas in short, medium and long term treatment.**

### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2014-003671-30    |
| Trial protocol           | ES                |
| Global end of trial date | 01 September 2016 |

### Results information

|                                   |  |
|-----------------------------------|--|
| Result version number             | v1 (current)   |
| This version publication date     | 04 June 2022   |
| First version publication date    | 04 June 2022   |
| Summary attachment (see zip file) | Evaluation of the safety and effectiveness of oral propranolol in patients with von Hippel-Lindau disease and retinal hemangioblastomas: phase III clinical trial (bmjophth-2018-000203.pdf) |

### Trial information

#### Trial identification

|                       |                 |
|-----------------------|-----------------|
| Sponsor protocol code | VHL-HOPE-2014-1 |
|-----------------------|-----------------|

#### Additional study identifiers

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

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Alianza VHL   |
| Sponsor organisation address | C/ SANTA MARTA, 24, OLÍAS DEL REY, Spain, 45280   |
| Public contact               | Susi Martínez Gómez, ALIANZA ESPAÑOLA DE FAMILIAS DE VON HIPPEL-LINDAU, 34 616050514, info@alianzavhl.org |
| Scientific contact           | Karina Villar, ALIANZA ESPAÑOLA DE FAMILIAS DE VON HIPPEL-LINDAU, 34 607680759, kvillar@jccm.es           |

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:

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**Results analysis stage**

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|  |                   |
|--|-------------------|
| Analysis stage                                       | Final             |
| Date of interim/final analysis                       | 01 September 2016 |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 01 September 2016 |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 01 September 2016 |
| Was the trial ended prematurely?                     | No                |

Notes:

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**General information about the trial**

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Main objective of the trial:

TO EVALUATE THE EFFECTIVENESS OF PROPRANOLOL IN CONTROLLING THE GROWTH OF PAPILLARY AND JUXTAPAPILLARY RETINAL HEMANGIOBLASTOMAS (HB)

Protection of trial subjects:

All patients had the mobile phone number of their ophthalmologist for possible consultations

Background therapy: -

Evidence for comparator:

No comparator treatment

|   |                                       |
|---|---------------------------------------|
| Actual start date of recruitment                          | 15 September 2014                     |
| Long term follow-up planned                               | Yes                                   |
| Long term follow-up rationale                             | Safety, Efficacy, Scientific research |
| Long term follow-up duration                              | 2 Years                               |
| Independent data monitoring committee (IDMC) involvement? | Yes                                   |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |          |
|--------------------------------------|----------|
| Country: Number of subjects enrolled | Spain: 7 |
| Worldwide total number of subjects   | 7        |
| EEA total number of subjects         | 7        |

Notes:

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**Subjects enrolled per age group**

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|   |   |
|---|---|
| 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)                 | 1 |
| Adults (18-64 years)                      | 6 |
| From 65 to 84 years                       | 0 |
| 85 years and over                         | 0 |

## Subject disposition

### Recruitment

Recruitment details:

The association of patients Alianza VHL informed about and invited their members to participate in the study.

Seven VHL patients from different regions of Spain were included. All of them had a positive genetic diagnosis of VHL.

### Pre-assignment

Screening details:

The participants should meet one of the following two criteria: Papillary or juxtapapillary hemangioblastomas, non-eligible for standard treatment (laser photocoagulation or cryotherapy) due to the high risk of iatrogenic visual loss. Peripheral retinal hemangioblastomas for which patients had rejected standard treatments.

### Period 1

|                              |                 |
|------------------------------|-----------------|
| Period 1 title               | Baseline period |
| Is this the baseline period? | Yes             |
| Allocation method            | Not applicable  |
| Blinding used                | Not blinded     |

### Arms

|           |               |
|-----------|---------------|
| Arm title | Treatment arm |
|-----------|---------------|

Arm description:

The pharmaceutical form and strength used was propranolol 40 mg, film-coated tablets, 1 every 8 hours up to a total dosage of 120 mg/day, achieved in 7–10 days. An experienced cardiologist in handling propranolol established the dosage regimen. The patients did not receive other treatments during the study.

|  |                           |
|--|---------------------------|
| Arm type                               | Experimental              |
| Investigational medicinal product name | Propranolol hydrochloride |
| Investigational medicinal product code |                           |
| Other name                             |                           |
| Pharmaceutical forms                   | Film-coated tablet        |
| Routes of administration               | Oral use                  |

Dosage and administration details:

propranolol 40 mg, film-coated tablets, 1 every 8 hours

|                                       |               |
|---------------------------------------|---------------|
| <b>Number of subjects in period 1</b> | Treatment arm |
| Started                               | 7             |
| Completed                             | 7             |

**Period 2**

|                              |                  |
|------------------------------|------------------|
| Period 2 title               | Final evaluation |
| Is this the baseline period? | No               |
| Allocation method            | Not applicable   |
| Blinding used                | Not blinded      |

**Arms**

|                  |               |
|------------------|---------------|
| <b>Arm title</b> | Treatment arm |
|------------------|---------------|

## Arm description:

The pharmaceutical form and strength used was propranolol 40 mg, film-coated tablets, 1 every 8 hours up to a total dosage of 120 mg/day, achieved in 7–10 days. An experienced cardiologist in handling propranolol established the dosage regimen. The patients did not receive other treatments during the study.

|  |                           |
|--|---------------------------|
| Arm type                               | Experimental              |
| Investigational medicinal product name | Propranolol hydrochloride |
| Investigational medicinal product code |                           |
| Other name                             |                           |
| Pharmaceutical forms                   | Film-coated tablet        |
| Routes of administration               | Oral use                  |

## Dosage and administration details:

propranolol 40 mg, film-coated tablets, 1 every 8 hours

| <b>Number of subjects in period 2</b> | Treatment arm |
|---------------------------------------|---------------|
| Started                               | 7             |
| Completed                             | 6             |
| Not completed                         | 1             |
| Physician decision                    | 1             |

## Baseline characteristics

## End points

### End points reporting groups

|  |               |
|--|---------------|
| Reporting group title  | Treatment arm |
| Reporting group description:<br>The pharmaceutical form and strength used was propranolol 40 mg, film-coated tablets, 1 every 8 hours up to a total dosage of 120 mg/day, achieved in 7–10 days. An experienced cardiologist in handling propranolol established the dosage regimen. The patients did not receive other treatments during the study. |               |
| Reporting group title  | Treatment arm |
| Reporting group description:<br>The pharmaceutical form and strength used was propranolol 40 mg, film-coated tablets, 1 every 8 hours up to a total dosage of 120 mg/day, achieved in 7–10 days. An experienced cardiologist in handling propranolol established the dosage regimen. The patients did not receive other treatments during the study. |               |

### Primary: Number and size of all the retinal hemangioblastomas

|   |   |  |  |  |
|---|---|--|--|--|
| End point title   | Number and size of all the retinal hemangioblastomas <sup>[1]</sup> |  |  |  |
| End point description:  |   |  |  |  |
|   |   |  |  |  |
| End point type  | Primary   |  |  |  |
| End point timeframe:  |   |  |  |  |
| The primary endpoint of the study was the number and size of all the retinal hemangioblastomas. The follow-up visits were scheduled at the Ophthalmology Department at baseline and at months 1, 3, 6, 9 and 12 of treatment. |   |  |  |  |
| 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: the number of patients and tumors is so small that statistical analysis is meaningless. This study has only a descriptive objective.   |   |  |  |  |
|   |   |  |  |  |
| End point values  | Treatment arm   |  |  |  |
| Subject group type  | Reporting group   |  |  |  |
| Number of subjects analysed   | 7   |  |  |  |
| Units: cm   |   |  |  |  |
| number (not applicable)   | 7   |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

At baseline, and at 1, 3, 6, 9 and 12 months

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | Treatment arm |
|-----------------------|---------------|

Reporting group description: -

| Serious adverse events                            | Treatment arm |  |  |
|---|---------------|--|--|
| Total subjects affected by serious adverse events |               |  |  |
| subjects affected / exposed                       | 0 / 7 (0.00%) |  |  |
| number of deaths (all causes)                     | 0             |  |  |
| number of deaths resulting from adverse events    | 0             |  |  |

Frequency threshold for reporting non-serious adverse events: 1 %

| Non-serious adverse events                            | Treatment arm  |  |  |
|---|----------------|--|--|
| Total subjects affected by non-serious adverse events |                |  |  |
| subjects affected / exposed                           | 1 / 7 (14.29%) |  |  |
| Vascular disorders                                    |                |  |  |
| Hypotension   |                |  |  |
| subjects affected / exposed                           | 1 / 7 (14.29%) |  |  |
| occurrences (all)                                     | 1              |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/31245608>