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:

Results analysis stage

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:

General information about the trial

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:

Population of trial subjects

Subjects enrolled per country

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

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)	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

Number of subjects in period 1	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

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

Number of subjects in period 2	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:

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:

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[1]

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

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/31245608