Clinical trial results:
STUDY TO EVALUATE THE PROPORTIONALITY OF 3 ORAL DOSES OF PIRLINDOLE IN HEALTHY VOLUNTEERS.

Summary

EudraCT number	2012-003090-26
Trial protocol	ES
Global end of trial date	02 May 2013

Results information

Result version number	v1 (current)
This version publication date	08 August 2020
First version publication date	08 August 2020

Trial information

Trial identification

Sponsor protocol code	110401

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Tecnimede, Sociedade Técnico-Medicinal, S.A.
Sponsor organisation address	Zona Industrial da Abrunheira, R. da Tapada Grande, nº 2, Sintra, Portugal, 2710-089
Public contact	SPONSOR'S REPRESENTATIVE, Tecnimede, Sociedade Técnico-Medicinal, S.A., +351 210414187, dmed.ct@tecnimede.pt
Scientific contact	SPONSOR'S REPRESENTATIVE, Tecnimede, Sociedade Técnico-Medicinal, S.A., +351 210414187, dmed.ct@tecnimede.pt

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	02 May 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 May 2013
Global end of trial reached?	Yes
Global end of trial date	02 May 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Main objective is to assess the proportionality of 3 pirlindole doses (50, 100 and 150 mg) administered orally in healthy volunteers.

Protection of trial subjects:

The study was conducted following the international recommendations for clinical research gathered in the declaration of Helsinki and its updating (revised in Tokyo 1975, Venice 1983, Hong Kong 1989, Sommerset West 1996, Edinburgh 2000, Washington 2002 and Seoul, South Korea 2008) and following the ICH Harmonized tripartite Guidelines for Good Clinical Practice (CPMP/ICH/135/95), guidelines of the Spanish Ministry of Health (Spanish Real Decret 223/2004) as well as the Directive 2001/20/EC (Note for Guidance "Good Clinical Practice for Studies on Medicinal Products in the European Community").

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 April 2013
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	Spain: 18
Worldwide total number of subjects	18
EEA total number of subjects	18

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)	18
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study participants were selected from the panel of volunteers at the Centre d' Investigació de Medicaments CIM-Sant Pau. The beginning of the study ("first subject in") was on 29 April 2013.

Pre-assignment

Screening details:

The screening was performed during the four weeks and the final evaluation was carried out the day after the administration of the medication. During the screening period (four weeks before the randomization) all participants gave their informed consent and underwent a screening check-up to verify that they met the inclusion/exclusion criteria.

Period 1

Period 1 title	Overall period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Pirlindole 50 mg

Arm description:

All participants who received Pirlindole (50mg) and who were not excluded from the pharmacokinetic population.

Arm type	Experimental
Investigational medicinal product name	Pirlindole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One single oral dose of Pirlindole 50 mg (one tablet of 50mg) was administered under fasting conditions. The medication was administrated with 240 ml of water.

Arm title	Pirlindole 100 mg

Arm description:

All participants who received Pirlindole (100 mg) and who were not excluded from the pharmacokinetic population.

Arm type	Experimental
Investigational medicinal product name	Pirlindole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One single oral dose of Pirlindole 100 mg (two tablets of 50mg) was administered under fasting conditions. The medication was administrated with 240 ml of water.

Arm title	Pirlindole 150 mg

Arm description:

All participants who received Pirlindole (150 mg) and who were not excluded from the pharmacokinetic population.

Arm type	Experimental

Investigational medicinal product name	Pirlindole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One single oral dose of Pirlindole 150 mg (three tablets of 50mg) was administered under fasting conditions. The medication was administrated with 240 ml of water.

Number of subjects in period 1	Pirlindole 50 mg	Pirlindole 100 mg	Pirlindole 150 mg
Started	6	6	6
Completed	6	6	6

Baseline characteristics

Reporting groups	
Reporting group title	Overall period

Reporting group description: -

Reporting group values	Overall period	Total	
Number of subjects	18	18	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	18	18	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	27.39		
standard deviation	± 7.55	-	
Gender categorical Units: Subjects			
Female	9	9	
Male	9	9	
Body weight Units: Kg			
arithmetic mean	66.57		
standard deviation	± 8.78	-	
Height Units: cm			
arithmetic mean	168.33		
standard deviation	± 6.31	-	
BMI: Quetelet’s index Units: kg/m2			
arithmetic mean	23.45		
standard deviation	± 2.52	-	

End points

End points reporting groups	
Reporting group title	Pirlindole 50 mg
Reporting group description:	
All participants who received Pirlindole (50mg) and who were not excluded from the pharmacokinetic population.	
Reporting group title	Pirlindole 100 mg
Reporting group description:	
All participants who received Pirlindole (100 mg) and who were not excluded from the pharmacokinetic population.	
Reporting group title	Pirlindole 150 mg
Reporting group description:	
All participants who received Pirlindole (150 mg) and who were not excluded from the pharmacokinetic population.	

Primary: Area under the plasma concentration curve (AUC) from time 0 to last observed concentration of Pirlindole	
End point title	Area under the plasma concentration curve (AUC) from time 0 to last observed concentration of Pirlindole
End point description:	
End point type	Primary
End point timeframe:	
Baseline (pre-dose), +10 min, +20 min, +30 min, +45 min, +1 h, +1h15 min, +1h30min, +1h45min, +2h, +3h, +5h, +6h, +8h, +12h and +24h post-dose.	

End point values	Pirlindole 50 mg	Pirlindole 100 mg	Pirlindole 150 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	6	
Units: ng.h/mL				
arithmetic mean (standard deviation)	55.84 (± 27.77)	301.62 (± 279.55)	370.23 (± 225.77)	

Statistical analyses

Statistical analysis title	Linear regression analysis
Comparison groups	Pirlindole 50 mg v Pirlindole 100 mg v Pirlindole 150 mg
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	other
Method	Regression, Linear
Parameter estimate	Coefficient of the regression line
Point estimate	1.715

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.976
upper limit	2.453

Primary: Maximum concentration (Cmax) in plasma of Pirlindole

End point title	Maximum concentration (Cmax) in plasma of Pirlindole

End point description:

End point type	Primary

End point timeframe:

Baseline (pre-dose), +10 min, +20 min, +30 min, +45 min, +1 h, +1h15 min, +1h30min, +1h45min, +2h, +3h, +5h, +6h, +8h, +12h and +24h post-dose.

End point values	Pirlindole 50 mg	Pirlindole 100 mg	Pirlindole 150 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	6	
Units: ng/mL				
arithmetic mean (standard deviation)	29.84 (± 16.46)	96.37 (± 65.18)	123.56 (± 62.71)	

Statistical analyses

Statistical analysis title	Linear regression analysis
Comparison groups	Pirlindole 50 mg v Pirlindole 100 mg v Pirlindole 150 mg
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	other
Method	Regression, Linear
Parameter estimate	Coefficient of the regression line
Point estimate	1.339
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.908

Primary: Area under the concentration-time curve from time 0 to infinity (AUC0-inf) in plasma of Pirlindole

End point title	Area under the concentration-time curve from time 0 to infinity (AUC0-inf) in plasma of Pirlindole

End point description:

End point type	Primary

End point timeframe:

Baseline (pre-dose), +10 min, +20 min, +30 min, +45 min, +1 h, +1h15 min, +1h30min, +1h45min, +2h, +3h, +5h, +6h, +8h, +12h and +24h post-dose.

End point values	Pirlindole 50 mg	Pirlindole 100 mg	Pirlindole 150 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	6	
Units: ng.h/mL				
arithmetic mean (standard deviation)	59.27 (± 30.74)	313.12 (± 292.99)	384.71 (± 239.73)	

Statistical analyses

Statistical analysis title	Linear regression analysis
Comparison groups	Pirlindole 50 mg v Pirlindole 100 mg v Pirlindole 150 mg
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	other
Method	Regression, Linear
Parameter estimate	Coefficient of the regression line
Point estimate	1.697
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	2.443

Secondary: Elimination rate constant (Kel) of Pirlindole

End point title	Elimination rate constant (Kel) of Pirlindole

End point description:

End point type	Secondary

End point timeframe:

Baseline (pre-dose), +10 min, +20 min, +30 min, +45 min, +1 h, +1h15 min, +1h30min, +1h45min, +2h, +3h, +5h, +6h, +8h, +12h and +24h post-dose.

End point values	Pirlindole 50 mg	Pirlindole 100 mg	Pirlindole 150 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	6	
Units: 1/h				
arithmetic mean (standard deviation)	0.37 (± 0.23)	0.25 (± 0.15)	0.18 (± 0.06)	

Statistical analyses

No statistical analyses for this end point

Secondary: Elimination half-life (T ½) of Pirlindole

End point title	Elimination half-life (T ½) of Pirlindole

End point description:

End point type	Secondary

End point timeframe:

Baseline (pre-dose), +10 min, +20 min, +30 min, +45 min, +1 h, +1h15 min, +1h30min, +1h45min, +2h, +3h, +5h, +6h, +8h, +12h and +24h post-dose.

End point values	Pirlindole 50 mg	Pirlindole 100 mg	Pirlindole 150 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	6	
Units: hour				
median (full range (min-max))	2.63 (1.05 to 4.79)	3.75 (1.43 to 6.16)	3.90 (2.81 to 7.28)	

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent volume of distribution estimated from extravascular route (Vd/F) of Pirlindole

End point title	Apparent volume of distribution estimated from extravascular route (Vd/F) of Pirlindole

End point description:

End point type	Secondary

End point timeframe:

Baseline (pre-dose), +10 min, +20 min, +30 min, +45 min, +1 h, +1h15 min, +1h30min, +1h45min, +2h, +3h, +5h, +6h, +8h, +12h and +24h post-dose.

End point values	Pirlindole 50 mg	Pirlindole 100 mg	Pirlindole 150 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	6	
Units: litre(s)				
arithmetic mean (standard deviation)	3133.18 (± 1068.80)	2288.59 (± 719.24)	2729.25 (± 785.49)	

Statistical analyses

No statistical analyses for this end point

Secondary: Total body clearance estimated from extravascular route (Cl/F) of Pirlindole

End point title	Total body clearance estimated from extravascular route (Cl/F) of Pirlindole

End point description:

End point type	Secondary

End point timeframe:

Baseline (pre-dose), +10 min, +20 min, +30 min, +45 min, +1 h, +1h15 min, +1h30min, +1h45min, +2h, +3h, +5h, +6h, +8h, +12h and +24h post-dose.

End point values	Pirlindole 50 mg	Pirlindole 100 mg	Pirlindole 150 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	6	
Units: L/h				
arithmetic mean (standard deviation)	1014.28 (± 427.14)	612.39 (± 436.59)	517.96 (± 275.17)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to reach maximum (peak) plasma concentration (Tmax) of Pirlindole

End point title	Time to reach maximum (peak) plasma concentration (Tmax) of Pirlindole

End point description:

End point type	Secondary

End point timeframe:

Baseline (pre-dose), +10 min, +20 min, +30 min, +45 min, +1 h, +1h15 min, +1h30min, +1h45min, +2h, +3h, +5h, +6h, +8h, +12h and +24h post-dose.

End point values	Pirlindole 50 mg	Pirlindole 100 mg	Pirlindole 150 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	6	
Units: hour				
median (full range (min-max))	0.75 (0.75 to 1.75)	1.0 (0.75 to 1.75)	1.25 (0.75 to 5.0)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Adverse Events are monitored from date of First Subject First Visit (FSFV) until Last Subject Last Visit (LSLV).	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups	
Reporting group title	Pirlindole 50 mg
Reporting group description: All participants who received Pirlindole (50mg) and who were not excluded from the pharmacokinetic population.	
Reporting group title	Pirlindole 100 mg
Reporting group description: All participants who received Pirlindole (100 mg) and who were not excluded from the pharmacokinetic population.	
Reporting group title	Pirlindole 150 mg
Reporting group description: All participants who received Pirlindole (150 mg) and who were not excluded from the pharmacokinetic population.	

Serious adverse events	Pirlindole 50 mg	Pirlindole 100 mg	Pirlindole 150 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Pirlindole 50 mg	Pirlindole 100 mg	Pirlindole 150 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 6 (33.33%)	1 / 6 (16.67%)	1 / 6 (16.67%)
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 6 (33.33%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	2	1	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