Clinical trial results:
Efficacy and safety of Lorista®, Lorista® H and Lorista® HD in the treatment of mild to moderate arterial hypertension

Summary

EudraCT number	2004-004933-32
Trial protocol	CZ
Global end of trial date	24 June 2004

Results information

Result version number	v1 (current)
This version publication date	03 July 2021
First version publication date	03 July 2021

Trial information

Trial identification

Sponsor protocol code	km 55/2004 – LORISTAH/CZ

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	protocol code in SI: km 54/2004 - LORISTAHHD/SI

Notes:

Sponsors

Sponsor organisation name	Krka, d.d., Novo mesto
Sponsor organisation address	Šmarješka cesta 6, Novo mesto, Slovenia, 8501
Public contact	Tanja Kohek, Krka, d.d., Novo mesto Dunajska cesta 65 1000 Ljubljana Slovenia, 00386 41 589769, tanja.kohek@krka.biz
Scientific contact	Tanja Kohek, Krka, d.d., Novo mesto Dunajska cesta 65 1000 Ljubljana Slovenia, 00386 41 589769, tanja.kohek@krka.biz
Sponsor organisation name	Krka ČR s.r.o.
Sponsor organisation address	Sokolovská 192/79, Prague, Czechia, 186 00
Public contact	Martin Sustr, Krka ČR s.r.o. Sokolovská 192/79 186 00 Prague Czechia, 00420 602 486846, martin.sustr@krka.biz
Scientific contact	Martin Sustr, Krka ČR s.r.o. Sokolovská 192/79 186 00 Prague Czechia, 00420 602 486846, martin.sustr@krka.biz

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric	No

investigation plan (PIP)	
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	31 March 2006
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 June 2004
Global end of trial reached?	Yes
Global end of trial date	24 June 2004
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of this trial is to confirm the antihypertensive effect of Lorista® tablets (50 mg of losartan), Lorista® H tablets (fixed dose combination of 50 mg of losartan and 12,5 mg of hydrochlorothiazide) and Lorista® HD (fixed dose combination of 100 mg of losartan and 25 mg of hydrochlorothiazide) in patients with mild to moderate hypertension:
• previously untreated or
• those with hypertension unsuccessfully treated with monotherapy or combination of antihypertensive drugs (fixed dose or non-fixed dose combinations) or
• in whom antihypertensive therapy needs to be changed due to adverse reactions experienced with previous antihypertensive therapy,
and to establish the tolerance and the effect of therapy on the patient’s quality of life.

Protection of trial subjects:

The patients were divided into two groups with regard to dosing. In the I. group of patients a starting dose was one tablet of Lorista®, after four weeks of treatment those patients, whose blood pressure did not respond properly (140/90 mmHg or less) continued the treatment with 1 tablet of Lorista® H. After eight weeks of treatment, those patients, whose blood pressure was not 140/90 mmHg or less, continued the treatment with 1 tablet of Lorista® plus 1 tablet of Lorista® H daily. After eleven weeks of treatment, those patients, whose blood pressure was not 140/90 mmHg or less, continued the treatment with one tablet of Lorista® HD daily.

In the II. group of patients starting dose was one tablet of Lorista® H, after four weeks of treatment, those patients, whose blood pressure did not respond properly (140/90 mmHg or less), continued the treatment with 1 tablet of Lorista® plus 1 tablet of Lorista® H daily. After eight weeks of treatment, those patients, whose blood pressure was not 140/90 mmHg or less, continued the treatment with 1 tablet of Lorista® HD daily.

Background therapy: -
Evidence for comparator: -

Actual start date of recruitment	15 April 2003
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	Czechia: 132
Country: Number of subjects enrolled	Slovenia: 221
Worldwide total number of subjects	353
EEA total number of subjects	353

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)	211
From 65 to 84 years	142
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

353 patients enrolled from Slovenia and Czechia. First patient in (FPI) was on 15.4.2003 and Last patient Out (LPO) was on 24.6.2004.

Pre-assignment

Screening details:

In general:
- Male and female adults from 18-80 years old with AH.
- In I. group were included previously untreated patients and patients with AH unsuccessfully treated with previous monotherapy (inefficacy or AR).
- In II. group were included patients with AH unsuccessfully treated with previous combination AH treatment (inefficacy or AR).

Period 1

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

Arms

Arm title	All patients

Arm description:

All patients enrolled in the study. A total of 353 patients were enrolled in the study in Slovenia and Czechia.

Arm type	Active comparator
Investigational medicinal product name	Lorista®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

One tablet of Lorista® contains 50 mg of losartan. The patient takes one tablet daily.

Investigational medicinal product name	Lorista® H
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

One tablet of Lorista® H contains 50 mg of losartan and 12.5 mg of hydrochlorothiazid. The patient takes one tablet daily.

Investigational medicinal product name	Lorista® HD
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

One tablet of Lorista® HD contains 100 mg of losartan and 25 mg of hydrochlorothiazid. The patient takes one tablet daily.

Number of subjects in period 1	All patients
Started	353
Completed	322
Not completed	31
Consent withdrawn by subject	8
Adverse event, non-fatal	5
Protocol deviation	18

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	353	353	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	60.3		
standard deviation	± 12.0	-	
Gender categorical Units: Subjects			
Female	209	209	
Male	144	144	

End points

End points reporting groups

Reporting group title	All patients

Reporting group description:

All patients enrolled in the study. A total of 353 patients were enrolled in the study in Slovenia and Czechia.

Primary: SBP and DBP on each visit

End point title	SBP and DBP on each visit[1]

End point description:

In the I. group of patients a starting dose was 1 tablet of Lorista®. After 4 weeks of treatment those patients, whose blood pressure was not 140/90 mmHg or less, continued the treatment with 1 tablet of Lorista® H. After 8 weeks of treatment, those patients, whose blood pressure was not 140/90 mmHg or less, continued the treatment with 1 tablet of Lorista® and 1 tablet of Lorista® H daily. After 11 weeks of treatment, those patients, whose blood pressure was not 140/90 mmHg or less, continued the treatment with one tablet of Lorista® HD daily.
In the II. group of patients starting dose was 1 tablet of Lorista® H, after 4 weeks of treatment, those patients, whose blood pressure was not 140/90 mmHg or less, continued the treatment with 1 tablet of Lorista® and 1 tablet of Lorista® H daily. After 8 weeks of treatment, those patients, whose blood pressure was not 140/90 mmHg or less, continued the treatment with 1 tablet of Lorista® HD daily.

End point type	Primary

End point timeframe:

Duration of the treatment was 14 weeks. First week from V1 to V2 was a washout period. During washout period patients weren`t taking any AH medications.

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: In order to report statistical analysis it is required to define at least two comparison groups. This was one arm study.
The following data were statistically processed: the largest and the smallest data, arithmetic mean of data with standard deviation of data and standard error of mean and the value of t variable in t-test. Patients prematurely discontinuing the trial due to adverse reactions were also included in the statistical analysis.

End point values	All patients			
Subject group type	Reporting group			
Number of subjects analysed	327			
Units: mmHG				
arithmetic mean (standard deviation)				
SBP V1	157 (± 13.7)			
SBP V2	159 (± 12.5)			
SBP V3	144.1 (± 13.8)			
SBP V4	138.2 (± 12.5)			
SBP V5	134.8 (± 10.3)			
SBP V6	133.4 (± 9.8)			
DBP V1	93.6 (± 8.2)			
DBP V2	95.4 (± 8)			
DBP V3	86.8 (± 8.7)			
DBP V4	83.3 (± 7.7)			
DBP V5	82 (± 7.1)			
DBP V6	81.4 (± 6.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change of SBP and DBP from baseline to visit

End point title	Absolute change of SBP and DBP from baseline to visit

End point description:

In the I. group of patients a starting dose was 1 tablet of Lorista®. After 4 weeks of treatment those patients, whose blood pressure was not 140/90 mmHg or less, continued the treatment with 1 tablet of Lorista® H. After 8 weeks of treatment, those patients, whose blood pressure was not 140/90 mmHg or less, continued the treatment with 1 tablet of Lorista® and 1 tablet of Lorista® H daily. After 11 weeks of treatment, those patients, whose blood pressure was not 140/90 mmHg or less, continued the treatment with one tablet of Lorista® HD daily.
In the II. group of patients starting dose was 1 tablet of Lorista® H, after 4 weeks of treatment, those patients, whose blood pressure was not 140/90 mmHg or less, continued the treatment with 1 tablet of Lorista® and 1 tablet of Lorista® H daily. After 8 weeks of treatment, those patients, whose blood pressure was not 140/90 mmHg or less, continued the treatment with 1 tablet of Lorista® HD daily.

End point type	Secondary

End point timeframe:

Duration of the treatment was 14 weeks. First week from V1 to V2 was a washout period. During washout period patients weren`t taking any AH medications.

End point values	All patients			
Subject group type	Reporting group			
Number of subjects analysed	327			
Units: mmHG				
arithmetic mean (standard deviation)				
SBP baseline-V3	-15.5 (± 13.7)			
SBP baseline-V4	-21.6 (± 15)			
SBP baseline-V5	-25 (± 13.8)			
SBP baseline-V6	-26 (± 13.9)			
DBP baseline-V3	-8.7 (± 8.9)			
DBP baseline-V4	-12.2 (± 8.7)			
DBP baseline-V5	-13.7 (± 8.7)			
DBP baseline-V6	-14.2 (± 8.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of therapeutic effect

End point title	Assessment of therapeutic effect

End point description:

At the end of the study, 88.8% of the patients had blood pressure 140/90 mmHg or less (assessed as very good); 6.2% of the patients had the systolic blood pressure reduced by at least 10 mmHg, and the diastolic pressure by at least 5 mmHg (assessed as good); 2.8% of the patients had only the systolic blood pressure reduced by at least 10 mmHg, or only the diastolic pressure by at least 5 mmHg (assessed as satisfactory); 2.2% of the patients had the systolic blood pressure reduced by less than 10 mmHg and the diastolic pressure by less than 5 mmHg (assessed as unsatisfactory).

End point type	Secondary

End point timeframe:

Duration of the treatment was up to 14 weeks.

End point values	All patients			
Subject group type	Reporting group			
Number of subjects analysed	327			
Units: percentage				
number (not applicable)				
Very Good	88.8			
Good	6.2			
Satisfactory	2.8			
Unsatisfactory	2.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of total clinical effect

End point title	Assessment of total clinical effect

End point description:

85.4% of the patients had blood pressure of 140/90 mmHg or less and were without AR (assessed as excellent); 3.7% of the patients had blood pressure of 140/90 mmHg or less and had mild adverse reactions (assessed as very good); 6.5% of the patients had the SBP reduced by at least 10 mmHg and the DBP by at least 5 mmHg and were without adverse reactions (assessed as good); 2.8% of the patients had blood pressure of 140/90 mmHg or less or SBP reduced by at least 10 mmHg or DBP by at least 5 mmHg and were accompanied with moderate adverse reactions or only SBP was reduced by at least 10 mmHg or only DBP by at least 5 mmHg without adverse reactions (assessed as satisfactory); 1.6% of the patients had blood pressure of 140/90 mmHg or less but had very serious adverse reactions that induced withdrawal of the treatment or the SBP was reduced by less than 10 mmHg and DBP by less than 5 mmHg or very serious adverse reactions that induced withdrawal of the treatment (assessed as unsatisfactory)

End point type	Secondary

End point timeframe:

Duration of the tratment was up to 14 weeks

End point values	All patients			
Subject group type	Reporting group			
Number of subjects analysed	327			
Units: percentage				
number (not applicable)				
Excellent	85.4			
Very Good	3.7			
Good	6.5			
Satisfactory	2.8			
Unsatisfactory	1.6			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AE reporting timeline for one patient was up to 14 weeks and was the same for the whole duration of the study (FPI: 15.4.2003, LPO: 24.6.2004).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	8.0

Reporting groups

Reporting group title	All patients

Reporting group description: -

Serious adverse events	All patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 353 (1.13%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Vascular disorders			
Angioedema			
subjects affected / exposed	1 / 353 (0.28%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertensive crisis			
subjects affected / exposed	1 / 353 (0.28%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	2 / 353 (0.57%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	All patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 353 (4.25%)		
Nervous system disorders			
Dizziness			
subjects affected / exposed	10 / 353 (2.83%)		
occurrences (all)	12		
Headache			
subjects affected / exposed	5 / 353 (1.42%)		
occurrences (all)	6		

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