Clinical trial results:
The AT1 receptor antagonist losartan for the prevention of excessive aortic root dilatation in children and adolescents with Marfan syndrom

Summary

EudraCT number	2009-016139-36
Trial protocol	AT
Global end of trial date	12 November 2024

Results information

Result version number	v1 (current)
This version publication date	30 January 2025
First version publication date	30 January 2025

Trial information

Trial identification

Sponsor protocol code	V1,11.05.2009

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medical University of Vienna
Sponsor organisation address	Waehringer Guertel 18-20, Vienna, Austria, 1090
Public contact	Medical University of Vienna Division of Pediatric Cardiology, Medical University of Vienna Division of Pediatric Cardiology, +43 14040032170, christiane.pees@meduniwien.ac.at
Scientific contact	Medical University of Vienna Division of Pediatric Cardiology, Medical University of Vienna Division of Pediatric Cardiology, +43 14040032170, christiane.pees@meduniwien.ac.at

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 November 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 November 2024
Global end of trial reached?	Yes
Global end of trial date	12 November 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The efficacy of the medication Losartan on the increase of the aorticroot diameter and vascular wall stiffness

Protection of trial subjects:

No painfull investigations, only echocardiography during routine check-ups

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 September 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 35
Worldwide total number of subjects	35
EEA total number of subjects	35

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)	2
Children (2-11 years)	14
Adolescents (12-17 years)	19
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

During clinical outpatient visit check-up for aortic root diameter z-Score >3 inclusion if patients and parents consented to medication (all) and as well study participation , between Z-score 0-2 if patients and parents were as well willing to take medication, then asking for study participation, if not normal routine observation of aortic size

Pre-assignment

Screening details:

clinically confirmed diagnosis of Marfan syndrome (Ghent criteria)

Period 1

Period 1 title	losartan group (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	losartan group

Arm description:

all patients receiving losartan treatment and consented to study participation

Arm type	Active comparator
Investigational medicinal product name	losartan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

starting dosage 0,2 mg/kg BID, augmentation weekly up to max 2 mg/kg/d or 150 mg total

Number of subjects in period 1	losartan group
Started	35
Completed	27
Not completed	8
Lost to follow-up	3
aortic root replacement operation	5

Baseline characteristics

Reporting groups	
Reporting group title	losartan group
Reporting group description:	
all patients receiving losartan treatment and consented to study participation	

Reporting group values	losartan group	Total	
Number of subjects	35	35	
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)	2	2	
Children (2-11 years)	14	14	
Adolescents (12-17 years)	19	19	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	12	12	
Male	23	23	

Subject analysis sets	
Subject analysis set title	efficacy of losartan in relation to aortic root growth
Subject analysis set type	Per protocol
Subject analysis set description:	
all 6 to 12 months echocardiographic investigation of ascending aortic diameters, normalisation of diameters regarding patients weight and height and calculation of the elasticity of the ascending aortic tissue	
Subject analysis set title	Analysis after 3 years of follow-up
Subject analysis set type	Per protocol
Subject analysis set description:	
3 years increase of Z-Score of the aortic root diameter	
Subject analysis set title	Analysis after 6 years of follow-up
Subject analysis set type	Per protocol
Subject analysis set description:	
all 6 to 12 months echocardiographic investigation of ascending aortic diameters, normalisation of diameters regarding patients weight and height and calculation of the elasticity of the ascending aortic tissue	

Reporting group values	efficacy of losartan in relation to aortic root growth	Analysis after 3 years of follow-up	Analysis after 6 years of follow-up
Number of subjects	35	29	28

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)	2		
Children (2-11 years)	14		
Adolescents (12-17 years)	19		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Gender categorical Units: Subjects			
Female	12		
Male	23		

End points

End points reporting groups

Reporting group title	losartan group
Reporting group description:	
all patients receiving losartan treatment and consented to study participation	
Subject analysis set title	efficacy of losartan in relation to aortic root growth
Subject analysis set type	Per protocol
Subject analysis set description:	
all 6 to 12 months echocardiographic investigation of ascending aortic diameters, normalisation of diameters regarding patients weight and height and calculation of the elasticity of the ascending aortic tissue	
Subject analysis set title	Analysis after 3 years of follow-up
Subject analysis set type	Per protocol
Subject analysis set description:	
3 years increase of Z-Score of the aortic root diameter	
Subject analysis set title	Analysis after 6 years of follow-up
Subject analysis set type	Per protocol
Subject analysis set description:	
all 6 to 12 months echocardiographic investigation of ascending aortic diameters, normalisation of diameters regarding patients weight and height and calculation of the elasticity of the ascending aortic tissue	

Primary: efficacy of losartan treatment on aortic root dilatation/growth

End point title	efficacy of losartan treatment on aortic root dilatation/growth
End point description:	
End point type	Primary
End point timeframe:	
Z-Score of aortic root diameter and its increase at 3 and 6 years of follow-up	

End point values	Analysis after 3 years of follow-up	Analysis after 6 years of follow-up		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	29	28		
Units: Z-Score of aortic root diameter				
arithmetic mean (standard error)	-0.004 (± 0.17)	0.15 (± 0.13)		

Statistical analyses

Statistical analysis title	Analysis primary endpoint
Comparison groups	Analysis after 3 years of follow-up v Analysis after 6 years of follow-up

Number of subjects included in analysis	57
Analysis specification	Post-hoc
Analysis type	equivalence
P-value	≤ 0.05
Method	t-test, 2-sided

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: 2009-2024	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	27

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: no adverse events related to medication

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 March 2013	Prolongation of follow-up period from 3 up to 10 years

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported