



Clinical trial results:

Core decompression versus core decompression followed by infusion of Iloprost in the treatment of non-traumatic avascular necrosis of the femoral head

Summary

EudraCT number	2020-000624-20
Trial protocol	DE
Global end of trial date	02 October 2024

Results information

Result version number	v1 (current)
This version publication date	03 January 2025
First version publication date	03 January 2025

Trial information

Trial identification

Sponsor protocol code	ILONA
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	DRKS-ID: DRKS00022404

Notes:

Sponsors

Sponsor organisation name	Universität Leipzig
Sponsor organisation address	Ritterstr. 26, Leipzig, Germany,
Public contact	ZKS Leipzig, Universität Leipzig, 49 341 97 16247, ilona@zks.uni-leipzig.de
Scientific contact	ZKS Leipzig, Universität Leipzig, 49 341 97 16247, ilona@zks.uni-leipzig.de

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	26 November 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 October 2024
Global end of trial reached?	Yes
Global end of trial date	02 October 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Primary objective of the ILONA trial is to show that in patients with non-traumatic avascular necrosis of the femoral head treatment with Iloprost for 10 days in addition to core decompression is more effective compared to core decompression alone with regard to functional outcome assessed by the Harris Hip Score (HHS) after 12 months.

Protection of trial subjects:

In the first 2-3 days of treatment, the individually tolerated dose must be determined. Blood pressure and heart rate checks are required at the beginning of the infusion and at each dose change (before or at start of new dosage).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 2021
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	Germany: 5
Worldwide total number of subjects	5
EEA total number of subjects	5

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)	5
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study aimed to include a total of 38 patients providing evaluable data on primary and secondary endpoints. During the study period, 17 patients were screened, of which 5 patients were randomized. The first patient was registered for the study on 27.04.2022 and the last patient visit took place on 09.10.2024.

Pre-assignment

Screening details:

Patients with N-ANFH were pre-screened: After the informed consent, MRI and X-ray images were evaluated by a core lab. If the patient was eligible acc. to the images, further screening took place.

Pre-assignment period milestones

Number of subjects started	5
Number of subjects completed	5

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

The trial is a double-blind trial. Iloprost was provided by the Sponsor to the trial site pharmacies, placebo was provided by the trial site pharmacies. Blinding was performed by the trial site pharmacy at the time of reconstitution. Blinding was performed following a randomisation list provided by the ZKS Leipzig and the pharmacy staff was instructed on how to perform blinding.

Arms

Are arms mutually exclusive?	Yes
Arm title	Iloprost

Arm description:

patients receiving Iloprost infusion after core decompression

Arm type	Experimental
Investigational medicinal product name	Iloprost
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Iloprost5 should be administered in a dose of max. 20 µg/day for 10 days.

In the first 2-3 days of treatment, the individually tolerated dose must be determined. The initial treatment should be started with an infusion rate of 0,5 ng/kg/min for half an hour. The dose should then be increased to 0,625 ng/kg/min and to a maximum of 0,75 ng/kg/min. The exact infusion rate, which is calculated based on body weight, should be set to 0,5, 0,625 or 0,75 ng/kg/ml. If side effects such as headaches and nausea or undesirable drop in blood pressure occur, the infusion rate should be reduced until the dose tolerated by the patient has been determined. In case of serious side effects, the infusion should be interrupted. With the tolerated dose determined in the first 2-3 days, treatment should then generally be continued.

Arm title	Placebo
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Arm description:

patients receiving saline solution infusion after core decompression

Arm type	Placebo
Investigational medicinal product name	Saline Solution (Placebo)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

The placebo is saline solution (0,9%) and the procedures for dosage and administration are identical with iloprost, since the trial is blinded.

Number of subjects in period 1	Iloprost	Placebo
Started	2	3
Baseline and Surgery	2	3
Hospital Stay	2	2
Follow-up (V1-V4)	2	2
Completed	2	2
Not completed	0	1
patient cancelled hospital stay (family reasons)	-	1

Baseline characteristics

Reporting groups

Reporting group title	Iloprost
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Reporting group description:

patients receiving Iloprost infusion after core decompression

Reporting group title	Placebo
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Reporting group description:

patients receiving saline solution infusion after core decompression
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Reporting group values	Iloprost	Placebo	Total
Number of subjects	2	3	5
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	2	3	5
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Mean			
Units: years			
arithmetic mean	43.5	37.3	
full range (min-max)	37 to 50	28 to 50	-
Gender categorical			
Units: Subjects			
Female	1	1	2
Male	1	2	3
ARCO Score			
Units: Subjects			
ARCO I	0	1	1
ARCO II	2	2	4

Subject analysis sets

Subject analysis set title	Full analysis set
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Subject analysis set type	Full analysis
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Subject analysis set description:

All patients analysed according to the randomisation result.
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Reporting group values	Full analysis set		
Number of subjects	5		
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)	5		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Mean			
Units: years			
arithmetic mean	39.8		
full range (min-max)	28 to 50		
Gender categorical			
Units: Subjects			
Female	2		
Male	3		
ARCO Score			
Units: Subjects			
ARCO I	1		
ARCO II	4		

End points

End points reporting groups

Reporting group title	Iloprost
Reporting group description: patients receiving Iloprost infusion after core decompression	
Reporting group title	Placebo
Reporting group description: patients receiving saline solution infusion after core decompression	
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis
Subject analysis set description: All patients analysed according to the randomisation result.	

Primary: Harris Hip Score

End point title	Harris Hip Score
End point description:	
End point type	Primary
End point timeframe: After 12 months (after Core Decompression surgery)	

End point values	Iloprost	Placebo	Full analysis set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	2	2 ^[1]	4	
Units: Score points				
HHS <70 (poor result)	0	1	1	
HHS 70-80 (fair)	0	1	1	
HHS 81-90 (good)	0	0	0	
HHS 91-100 (excellent)	2	0	2	

Notes:

[1] - one patient dropped out before the documentation of the primary endpoint

Statistical analyses

Statistical analysis title	reporting of single values
Statistical analysis description: Due to the small amount of patients that were recruited, the results are only reported in a descriptive manner.	
Comparison groups	Iloprost v Placebo v Full analysis set
Number of subjects included in analysis	8
Analysis specification	Pre-specified
Analysis type	other ^[2]
P-value	< 0.05 ^[3]
Method	no tests applicable
Parameter estimate	no parameter applicable
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0
Variability estimate	Standard deviation
Dispersion value	0

Notes:

[2] - Due to the small amount of patients that were recruited, the results are only reported in a descriptive manner.

[3] - The planned tests were not applicable due to the small number of recruited patients.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were documented on special AE-forms from start of the core decompression surgery until 4 weeks after the last application of Iloprost/placebo.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.0
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Reporting groups

Reporting group title	Iloprost
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Reporting group description: -

Reporting group title	Placebo
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Reporting group description: -

Serious adverse events	Iloprost	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Iloprost	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)	2 / 3 (66.67%)	
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Pregnancy, puerperium and perinatal conditions			
Abortion early			

subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 3 (33.33%) 1	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	1 / 2 (50.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Colitis ulcerative			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Sleep apnoea syndrome			
subjects affected / exposed	0 / 2 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 February 2022	documentation of sociodemographic factors added at baseline, evaluation of outcome scores at V1 deleted, since these are evaluated at V2.
06 June 2023	trial indication was expanded from "idiopathic non-traumatic avascular necrosis of the femoral head" to "non-traumatic avascular necrosis of the femoral head". Pathogenesis does not play a determining role in the therapy and outcomes considered in the trial. Thus, the trial indication was no longer restricted to idiopathic pathogenesis and this indication extension was also indicated in the trial title. Restrictions regarding the treated side of the hip (more vs. less effected) were changed. The maximum age for eligible patients was changed from 50 to 65 with the note to rule out the differential diagnosis of rapidly destructive osteoarthritis in patients above 50 years of age. Exclusion criterium "known aetiologies" was changed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The trial only recruited 5 instead of 38 patients. Therefore, the recruitment was terminated early and the results are only reported in a descriptive manner.

Notes: