



Clinical trial results: EVALUATION OF CEREBRAL THROMBOEMBOLISM AFTER TAVR Summary

EudraCT number	2016-001777-33
Trial protocol	DE
Global end of trial date	02 August 2018

Results information

Result version number	v1 (current)
This version publication date	04 June 2022
First version publication date	04 June 2022

Trial information

Trial identification

Sponsor protocol code	EARTH-TAVR01
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02758964
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Charité Universitätsmedizin Berlin
Sponsor organisation address	HIndenburgdamm 30 , Berlin, Germany, 12203
Public contact	Clinical Trials Contact, Department of Cardiology, 0049 030450513702, ulf.landmesser@charite.de
Scientific contact	Clinical Trials Contact, Department of Cardiology, 0049 030450513702, ulf.landmesser@charite.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	03 December 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 August 2018
Global end of trial reached?	Yes
Global end of trial date	02 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the occurrence and extent of cerebral embolization (total new lesion volume) in patients before TAVR versus 3 months after TAVR by cerebral MRI scans.

The EARTH TAVR study investigates cerebral emboli by MRI, neurocognitive function and includes a neurological examination before TAVR, 1-2 days and 3 months after TAVR in conjunction with the GALILEO study (where patients are randomised to anticoagulation or DAPT after TAVI). In this way, a distinction can be made between procedural events directly associated with TAVR and events that could have been avoided in the course of the procedure (embolisms associated with undetected atrial fibrillation, thrombotic deposits on the valve prosthesis, etc.).

Protection of trial subjects:

- accurate selection of trial subjects according to inclusion and exclusion criteria
- follow-up visits to assess concomitant drug therapy and assess potential drug interactions and take early action
- follow-up visits to assess (serious) adverse events

Background therapy:

There is no specific treatment in connection to the EARTH TAVR trial. However, the GALILEO study assesses two antithrombotic strategies post-successful TAVR and treatments and dosing details of the GALILEO trial are described in its study protocol.

Evidence for comparator:

here is no specific treatment in connection to the EARTH TAVR trial. However, the GALILEO study assesses two antithrombotic strategies post-successful TAVR and treatments and dosing details of the GALILEO trial are described in its study protocol.

Actual start date of recruitment	01 July 2016
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	Germany: 55
Worldwide total number of subjects	55
EEA total number of subjects	55

Notes:

Subjects enrolled per age group

In utero	0
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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)	3
From 65 to 84 years	41
85 years and over	11

Subject disposition

Recruitment

Recruitment details:

The recruitment of 54 study participants was ongoing from 2016-2018 in Germany.

Pre-assignment

Screening details:

pre-TAVR assignment as part of clinical routine: TTE, angiogram, TAVR CT

Period 1

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

Blinding implementation details:

this is an observational study as sub-study of the randomized-controlled, not blinded GALILEO trial. In the observational period of the EARTH TAVR study, there is no blinding implementation.

Arms

Arm title	MRI, neurocognitive testing
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Arm description:

trial subjects received cerebral MRI and extensive neurocognitive testing.

Arm type	Experimental
Investigational medicinal product name	RIVAROXABAN
Investigational medicinal product code	366789-02-8
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

not applicable. SEE study GALILEO trial

Number of subjects in period 1	MRI, neurocognitive testing
Started	55
Completed	55

Baseline characteristics

Reporting groups

Reporting group title	overall trial
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Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	55	55	
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	79.4		
standard deviation	± 5.8	-	
Gender categorical			
Units: Subjects			
Female	42	42	
Male	13	13	

End points

End points reporting groups

Reporting group title	MRI, neurocognitive testing
Reporting group description: trial subjects received cerebral MRI and extensive neurocognitive testing.	
Subject analysis set title	Δ 90 days vs post TAVR FUP
Subject analysis set type	Intention-to-treat
Subject analysis set description: FUP, Follow-up	
Subject analysis set title	Δ 90 days FUP vs baseline
Subject analysis set type	Intention-to-treat
Subject analysis set description: FUP, Follow-up	

Primary: Δ post TAVR vs baseline

End point title	Δ post TAVR vs baseline
End point description: Change of the Diffusion-weighted imaging (DWI) volume	
End point type	Primary
End point timeframe: from baseline up to 48h post TAVR	

End point values	MRI, neurocognitive testing	Δ 90 days vs post TAVR FUP	Δ 90 days FUP vs baseline	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	28	25	30	
Units: cm ³				
arithmetic mean (confidence interval 95%)	0.32 (0.12 to 0.67)	-.37 (-0.68 to -0.13)	0 (0 to 0)	

Statistical analyses

Statistical analysis title	Change of the Diffusion-weighted imaging volume
Comparison groups	MRI, neurocognitive testing v Δ 90 days vs post TAVR FUP v Δ 90 days FUP vs baseline
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.025
Method	Logrank

Secondary: AIR Imaging lesions

End point title	AIR Imaging lesions
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End point description:

FLAIR, the fluidattenuated inversion recovery;

End point type	Secondary
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End point timeframe:

48h post-TAVR

End point values	MRI, neurocognitive testing			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: Count				
arithmetic mean (confidence interval 95%)	3.5 (2 to 7)			

Statistical analyses

No statistical analyses for this end point

Secondary: FLAIR Imaging volume

End point title	FLAIR Imaging volume
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End point description:

End point type	Secondary
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End point timeframe:

90 days after TAVR; Follow up

End point values	MRI, neurocognitive testing			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: volume cm ³				
arithmetic mean (confidence interval 95%)	0.11 (0.07 to 0.34)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

baseline until 3 months

Assessment type	Systematic
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Dictionary used

Dictionary name	own
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Dictionary version	1
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Reporting groups

Reporting group title	MRI, neurocognitive testing
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Reporting group description: -

Serious adverse events	MRI, neurocognitive testing		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 55 (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	MRI, neurocognitive testing		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 55 (0.00%)		

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 AEs and SAEs were reported.

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/34474587>