Clinical trial results:
Effect of Tadalafil on cerebral large arteries in stroke patients.

Summary

EudraCT number	2016-000896-26
Trial protocol	DK
Global end of trial date	04 August 2017

Results information

Result version number	v1 (current)
This version publication date	09 May 2020
First version publication date	09 May 2020

Trial information

Trial identification

Sponsor protocol code	ETLAS

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02801032
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Herlev Gentofte Hospital
Sponsor organisation address	Borgmester Ib Juuls Vej 1, Herlev, Denmark, 2730
Public contact	Christina Rostrup Kruuse, Herlev Gentofte Hospital, 45 38681233, christina.rostrup.kruuse@regionh.dk
Scientific contact	Christina Rostrup Kruuse, Herlev Gentofte Hospital, 45 38681233, christina.rostrup.kruuse@regionh.dk

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	29 January 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 August 2017
Global end of trial reached?	Yes
Global end of trial date	04 August 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective was to investigate the effect of the phosphodiesterase-5-inhibitor (PDE-5-inhibitor) tadalafil on blood flow velocity in the cerebral large arteries and cortical brain oxygenation in patients with former lacunar stroke caused by small vessel diseases.

Protection of trial subjects:

During the trial days, trial participants were monitored thoroughly with heart rate and blood pressure. They were asked how they felt every hour during the trial days and if they experienced any side effects. After the trial days, they were asked to complete a side effect form and then hand it in to the investigator. They were also given a phone number to the Department of Neurology, Herlev Gentofte Hospital (sponsor) which they could call to if they experienced any side effects or had any other trouble. If the participants experienced pain or distress during the trial days, we talked about it and tried to accomodate their wishes to see if we could minimize pain.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2016
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	Denmark: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	8

From 65 to 84 years	11
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

All patients were recruited from the Department of Neurology, Herlev Gentofte Hospital, Denmark. Patients were recruited year 2016 and 2017.

Pre-assignment

Screening details:

Evaluation by a doctor.

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, Monitor, Data analyst

Blinding implementation details:

Medication were packed in opaque capsuels by the pharmacy. The investigator and subjects were blinded from treatment. Data were analyzed in a blidend fashion. Unbliding was done after data had been analyzed.

Arms

Are arms mutually exclusive?	No
Arm title	Tadalafil

Arm description:

Crossover trial.
Tadalafil (20 mg) was given as a single dose during trial day one or two. Placebo was given on the other trial day.

Arm type	Experimental
Investigational medicinal product name	Tadalafil
Investigational medicinal product code	
Other name	Cialis
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Dosage: 20 mg.
Use: Oral use.
Single dose tadalafil was given on either trial day one or two.

Arm title	Placebo

Arm description:

Crossover trial. Placebo was given as a single dose during trial day one or two. Tadalafil was given on the other trial day.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Dosage: placebo
Administration details: Oral use
Single dose placebo was given on either trial day one or two.

Number of subjects in period 1	Tadalafil	Placebo
Started	20	20
Completed	19	20
Not completed	1	0
Adverse event, non-fatal	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial
Reporting group description:	
In this crossover trial, 20 subjects were recruited.	

Reporting group values	Overall trial	Total	
Number of subjects	20	20	
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)	8	8	
From 65-84 years	11	11	
85 years and over	1	1	
Gender categorical Units: Subjects			
Female	3	3	
Male	17	17	

End points

End points reporting groups

Reporting group title	Tadalafil
Reporting group description:	
Crossover trial. Tadalafil (20 mg) was given as a single dose during trial day one or two. Placebo was given on the other trial day.	
Reporting group title	Placebo
Reporting group description:	
Crossover trial. Placebo was given as a single dose during trial day one or two. Tadalafil was given on the other trial day.	
Subject analysis set title	Tadalafil - baseline
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Tadalafil baseline	
Subject analysis set title	Tadalafil - 30 minutes
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Tadalafil group at 30 minutes	
Subject analysis set title	Tadalafil - 60 minutes
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Tadalafil group at 60 minutes	
Subject analysis set title	Tadalafil - 90 minutes
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Tadalafil group at 90 minutes	
Subject analysis set title	Tadalafil - 120 minutes
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Tadalafil group at 120 minutes	
Subject analysis set title	Tadalafil - 150 minutes
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Tadalafil group at 150 minutes	
Subject analysis set title	Tadalafil - 180 minutes
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Tadalafil group at 180 minutes	
Subject analysis set title	Placebo - baseline
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Placebo group at baseline	
Subject analysis set title	Placebo - 30 minutes
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Placebo group at 30 minutes	
Subject analysis set title	Placebo - 60 minutes
Subject analysis set type	Sub-group analysis

Subject analysis set description: Placebo group at 60 minutes	
Subject analysis set title	Placebo - 90 minutes
Subject analysis set type	Sub-group analysis
Subject analysis set description: Placebo group at 90 minutes	
Subject analysis set title	Placebo - 120 minutes
Subject analysis set type	Sub-group analysis
Subject analysis set description: Placebo group at 120 minutes	
Subject analysis set title	Placebo - 150 minutes
Subject analysis set type	Sub-group analysis
Subject analysis set description: Placebo group at 150 minutes	
Subject analysis set title	Placebo - 180 minutes
Subject analysis set type	Sub-group analysis
Subject analysis set description: Placebo group at 180 minutes	

Primary: Transcranial Doppler

End point title	Transcranial Doppler

End point description:

Changes in mean blood flow velocity in the middle cerebral artery before and after tadalafil/placebo for each subject were calculated and then further used for statistical analysis. Here, results are shown as the mean value and standard deviation for both groups at the different timepoints.

End point type	Primary

End point timeframe:

We performed TCD measurements twice at baseline and after 30, 60, 90, 120, 150, and 180 minutes post-medication.

End point values	Tadalafil - baseline	Tadalafil - 30 minutes	Tadalafil - 60 minutes	Tadalafil - 90 minutes
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	19	19	19
Units: cm/sec				
arithmetic mean (standard deviation)	57.8 (± 10.8)	57.8 (± 10.4)	57.4 (± 10.1)	58.0 (± 11.7)

End point values	Tadalafil - 120 minutes	Tadalafil - 150 minutes	Tadalafil - 180 minutes	Placebo - baseline
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	19	19	20
Units: cm/sec				
arithmetic mean (standard deviation)	59.2 (± 12.7)	59.2 (± 12.7)	58.4 (± 12.0)	57.1 (± 11.1)

End point values	Placebo - 30 minutes	Placebo - 60 minutes	Placebo - 90 minutes	Placebo - 120 minutes
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	20	20	20
Units: cm/sec				
arithmetic mean (standard deviation)	59.3 (± 12.7)	58.7 (± 13.2)	59.6 (± 14.7)	59.9 (± 12.9)

End point values	Placebo - 150 minutes	Placebo - 180 minutes		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	20		
Units: cm/sec				
arithmetic mean (standard deviation)	59.8 (± 13.2)	59.7 (± 13.8)		

Statistical analyses

Statistical analysis title	ANOVA
Statistical analysis description:	
Total number of subjects: 19 in tadalafil and 20 in placebo.	
Comparison groups	Tadalafil - baseline v Tadalafil - 30 minutes v Tadalafil - 60 minutes v Tadalafil - 90 minutes v Tadalafil - 120 minutes v Tadalafil - 150 minutes v Tadalafil - 180 minutes v Placebo - baseline v Placebo - 30 minutes v Placebo - 60 minutes v Placebo - 90 minutes v Placebo - 120 minutes v Placebo - 150 minutes v Placebo - 180 minutes
Number of subjects included in analysis	273
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.05
Method	ANOVA

Notes:

[1] - We performed a repeated measurement analysis of variance (ANOVA).

Statistical analysis title	T-test
Statistical analysis description:	
Total number of subjects: 19 in tadalafil and 20 in placebo.	
Comparison groups	Tadalafil - baseline v Tadalafil - 30 minutes v Tadalafil - 60 minutes v Tadalafil - 90 minutes v Tadalafil - 120 minutes v Tadalafil - 150 minutes v Tadalafil - 180 minutes v Placebo - baseline v Placebo - 30 minutes v Placebo - 60 minutes v Placebo - 90 minutes v Placebo - 120 minutes v Placebo - 150 minutes v Placebo - 180 minutes

Number of subjects included in analysis	273
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	< 0.05
Method	t-test, 2-sided

Notes:

[2] - We performed a paired sample T-test when ANOVA detected a significant difference.

Primary: Near infrared spectroscopy

End point title	Near infrared spectroscopy

End point description:

Changes in cortical blood oxygen saturation before and after tadalafil/placebo for each subject were calculated and then further used for statistical analysis. Here, results are shown as the mean value and standard deviation for both groups at the different timepoints.

End point type	Primary

End point timeframe:

We performed NIRS measurements at baseline and after 30, 60, 90, 120, 150, and 180 minutes post-medication.

End point values	Tadalafil - baseline	Tadalafil - 30 minutes	Tadalafil - 60 minutes	Tadalafil - 90 minutes
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	19	19	19
Units: percent				
arithmetic mean (standard deviation)	66.8 (± 8.8)	66.7 (± 8.0)	66.6 (± 8.7)	67.2 (± 8.4)

End point values	Tadalafil - 120 minutes	Tadalafil - 150 minutes	Tadalafil - 180 minutes	Placebo - baseline
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	19	19	20
Units: percent				
arithmetic mean (standard deviation)	67.8 (± 8.5)	67.9 (± 9.0)	66.8 (± 9.0)	67.2 (± 7.7)

End point values	Placebo - 30 minutes	Placebo - 60 minutes	Placebo - 90 minutes	Placebo - 120 minutes
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	20	20	20
Units: percent				
arithmetic mean (standard deviation)	68.1 (± 8.2)	68.1 (± 7.8)	67.9 (± 7.4)	68.1 (± 7.0)

End point values	Placebo - 150 minutes	Placebo - 180 minutes		

Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	20		
Units: percent				
arithmetic mean (standard deviation)	68.0 (± 7.8)	67.7 (± 8.1)		

Statistical analyses

Statistical analysis title	ANOVA

Statistical analysis description:

Total number of subjects: 19 in tadalafil and 20 in placebo.

Comparison groups	Tadalafil - baseline v Tadalafil - 30 minutes v Tadalafil - 60 minutes v Tadalafil - 90 minutes v Tadalafil - 120 minutes v Tadalafil - 150 minutes v Tadalafil - 180 minutes v Placebo - baseline v Placebo - 30 minutes v Placebo - 60 minutes v Placebo - 90 minutes v Placebo - 120 minutes v Placebo - 150 minutes v Placebo - 180 minutes
Number of subjects included in analysis	273
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	< 0.05
Method	ANOVA

Notes:

[3] - We performed a repeated measurement analysis of variance (ANOVA).

Statistical analysis title	T-test

Statistical analysis description:

Total number of subjects: 19 in tadalafil and 20 in placebo.

Comparison groups	Tadalafil - baseline v Tadalafil - 30 minutes v Tadalafil - 60 minutes v Tadalafil - 90 minutes v Tadalafil - 120 minutes v Tadalafil - 150 minutes v Tadalafil - 180 minutes v Placebo - baseline v Placebo - 30 minutes v Placebo - 60 minutes v Placebo - 90 minutes v Placebo - 120 minutes v Placebo - 150 minutes v Placebo - 180 minutes
Number of subjects included in analysis	273
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	< 0.05
Method	t-test, 2-sided

Notes:

[4] - We performed a paired sample T-test when ANOVA detected a significant difference.

Secondary: Blood pressure - systolic

End point title	Blood pressure - systolic

End point description:

Changes in blood pressure before and after tadalafil/placebo for each subject were calculated and then further used for statistical analysis. Here, results are shown as the mean value and standard deviation for both groups at the different timepoints.

End point type	Secondary

End point timeframe:

We performed blood pressure measurements twice at baseline and after 60, 120, and 180 minutes post-medication.

End point values	Tadalafil - baseline	Tadalafil - 60 minutes	Tadalafil - 120 minutes	Tadalafil - 180 minutes
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	19	19	19
Units: mmHg				
arithmetic mean (standard deviation)	145.3 (± 16.9)	136.4 (± 17.4)	141.7 (± 20.0)	140.5 (± 14.5)

End point values	Placebo - baseline	Placebo - 60 minutes	Placebo - 120 minutes	Placebo - 180 minutes
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	20	20	20
Units: mmHg				
arithmetic mean (standard deviation)	146.3 (± 22.1)	142.5 (± 18.4)	143.8 (± 17.5)	147.1 (± 18.3)

Statistical analyses

Statistical analysis title	ANOVA
Statistical analysis description:	
Total number of subjects: 19 in tadalafil and 20 in placebo.	
Comparison groups	Tadalafil - baseline v Tadalafil - 60 minutes v Tadalafil - 120 minutes v Tadalafil - 180 minutes v Placebo - baseline v Placebo - 60 minutes v Placebo - 120 minutes v Placebo - 180 minutes
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	< 0.05
Method	ANOVA

Notes:

[5] - We performed a repeated measurment analysis of variance (ANOVA).

Statistical analysis title	T-test
Statistical analysis description:	
Total number of subjects: 19 in tadalafil and 20 in placebo.	
Comparison groups	Tadalafil - baseline v Tadalafil - 60 minutes v Tadalafil - 120 minutes v Tadalafil - 180 minutes v Placebo - baseline v Placebo - 60 minutes v Placebo - 120 minutes v Placebo - 180 minutes
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	other[6]
P-value	< 0.05
Method	t-test, 2-sided

Notes:

[6] - We performed a paired sample T-test when ANOVA detected a significant difference.

Secondary: Blood pressure - diastolic

End point title	Blood pressure - diastolic

End point description:

Changes in blood pressure before and after tadalafil/placebo for each subject were calculated and then further used for statistical analysis. Here, results are shown as the mean value and standard deviation for both groups at the different timepoints.

End point type	Secondary

End point timeframe:

We performed blood pressure measurements twice at baseline and after 60, 120, and 180 minutes post-medication.

End point values	Tadalafil - baseline	Tadalafil - 60 minutes	Tadalafil - 120 minutes	Tadalafil - 180 minutes
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	19	19	19
Units: mmHg				
arithmetic mean (standard deviation)	83.6 (± 9.1)	78.5 (± 9.6)	78.7 (± 10.2)	78.4 (± 10.2)

End point values	Placebo - baseline	Placebo - 60 minutes	Placebo - 120 minutes	Placebo - 180 minutes
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	20	20	20
Units: mmHg				
arithmetic mean (standard deviation)	79.0 (± 8.8)	80.3 (± 10.5)	79.5 (± 9.0)	82.0 (± 8.1)

Statistical analyses

Statistical analysis title	ANOVA

Statistical analysis description:

Total number of subjects: 19 in tadalafil and 20 in placebo.

Comparison groups	Tadalafil - baseline v Tadalafil - 60 minutes v Tadalafil - 120 minutes v Tadalafil - 180 minutes v Placebo - baseline v Placebo - 60 minutes v Placebo - 120 minutes v Placebo - 180 minutes
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	other[7]
P-value	> 0.05
Method	ANOVA

Notes:

[7] - We performed a repeated measurement analysis of variance (ANOVA).

Statistical analysis title	T-test

Statistical analysis description:

Total number of subjects: 19 in tadalafil and 20 in placebo.

Comparison groups	Tadalafil - baseline v Tadalafil - 60 minutes v Tadalafil - 120 minutes v Tadalafil - 180 minutes v Placebo - baseline v Placebo - 60 minutes v Placebo - 120 minutes v Placebo - 180 minutes
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	other[8]
P-value	< 0.05
Method	t-test, 2-sided

Notes:

[8] - We performed a paired sample T-test when ANOVA detected a significant difference.

Secondary: Heart rate

End point title	Heart rate

End point description:

Changes in heart rate before and after tadalafil/placebo for each subject were calculated and then further used for statistical analysis. Here, results are shown as the mean value and standard deviation for both groups at the different timepoints.

End point type	Secondary

End point timeframe:

We performed heart rate measurements twice at baseline and after 60, 120, and 180 minutes post-medication.

End point values	Tadalafil - baseline	Tadalafil - 60 minutes	Tadalafil - 120 minutes	Tadalafil - 180 minutes
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	19	19	19
Units: bpm				
arithmetic mean (standard deviation)	61.2 (± 11.8)	59.1 (± 9.8)	57.7 (± 9.2)	57.1 (± 9.2)

End point values	Placebo - baseline	Placebo - 60 minutes	Placebo - 120 minutes	Placebo - 180 minutes
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	20	20	20
Units: bpm				
arithmetic mean (standard deviation)	63.5 (± 11.7)	60.7 (± 10.4)	58.2 (± 9.9)	60.1 (± 9.9)

Statistical analyses

Statistical analysis title	ANOVA

Statistical analysis description:

Total number of subjects: 19 in tadalafil and 20 in placebo.

Comparison groups	Tadalafil - baseline v Tadalafil - 60 minutes v Tadalafil - 120 minutes v Tadalafil - 180 minutes v Placebo - baseline v Placebo - 60 minutes v Placebo - 120 minutes v Placebo - 180 minutes
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	other[9]
P-value	< 0.05
Method	ANOVA

Notes:

[9] - We performed a repeated measurement analysis of variance (ANOVA).

Secondary: EndoPAT - RHI

End point title	EndoPAT - RHI

End point description:

Changes in regional hyperemia index before and after tadalafil/placebo for each subject were calculated and then further used for statistical analysis. Here, results are shown as the mean value and standard deviation for both groups at the different timepoints.

End point type	Secondary

End point timeframe:

We performed EndoPAT measurements at baseline and after 180 minutes post-medication.

End point values	Tadalafil - baseline	Tadalafil - 180 minutes	Placebo - baseline	Placebo - 180 minutes
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	19	20	20
Units: no unit				
arithmetic mean (standard deviation)	2.4 (± 0.8)	2.6 (± 0.8)	2.4 (± 0.8)	2.6 (± 0.7)

Statistical analyses

Statistical analysis title	T-test

Statistical analysis description:

Total number of subjects: 19 in tadalafil and 20 in placebo.

Comparison groups	Tadalafil - baseline v Tadalafil - 180 minutes v Placebo - baseline v Placebo - 180 minutes
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	other[10]
P-value	< 0.05
Method	t-test, 2-sided

Notes:

[10] - We performed a paired sample T-test.

Secondary: EndoPat - AI

End point title	EndoPat - AI

End point description:

Changes in EndoPAT - augmentation index before and after tadalafil/placebo for each subject were calculated and then further used for statistical analysis. Here, results are shown as the mean value and standard deviation for both groups at the different timepoints.

End point type	Secondary

End point timeframe:

We performed EndoPAT measurements at baseline and after 180 minutes post-medication.

End point values	Tadalafil - baseline	Tadalafil - 180 minutes	Placebo - baseline	Placebo - 180 minutes
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	19	20	20
Units: no unit				
arithmetic mean (standard deviation)	25.2 (± 19.1)	29.0 (± 21.1)	21.2 (± 14.3)	28.1 (± 23.8)

Statistical analyses

Statistical analysis title	T-test

Statistical analysis description:

Total number of subjects: 19 in tadalafil and 20 in placebo.

Comparison groups	Tadalafil - baseline v Tadalafil - 180 minutes v Placebo - baseline v Placebo - 180 minutes
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	other[11]
P-value	< 0.05
Method	t-test, 2-sided

Notes:

[11] - We performed a paired sample T-test.

Secondary: EndoPAT - AI@75

End point title	EndoPAT - AI@75

End point description:

Changes in EndoPAT - augmentation index standardized to a heart rate of 75 before and after tadalafil/placebo for each subject were calculated and then further used for statistical analysis. Here, results are shown as the mean value and standard deviation for both groups at the different timepoints.

End point type	Secondary

End point timeframe:

We performed EndoPAT measurements at baseline and after 180 minutes post-medication.

End point values	Tadalafil - baseline	Tadalafil - 180 minutes	Placebo - baseline	Placebo - 180 minutes
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	19	20	20
Units: no unit				
arithmetic mean (standard deviation)	15.9 (± 17.5)	18.9 (± 19.3)	13.6 (± 12.0)	19.8 (± 21.0)

Statistical analyses

Statistical analysis title	T-test
Statistical analysis description:	
Total number of subjects: 19 in tadalafil and 20 in placebo.	
Comparison groups	Tadalafil - 180 minutes v Tadalafil - baseline v Placebo - baseline v Placebo - 180 minutes
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	other[12]
P-value	< 0.05
Method	t-test, 2-sided

Notes:

[12] - We performed a paired sample T-test.

Secondary: Blood sample - E-selectin

End point title	Blood sample - E-selectin
End point description:	
Changes in biomarker concentration before and after tadalafil/placebo for each subject were calculated and then further used for statistical analysis. Here, results are shown as the mean value and standard deviation for both groups at the different timepoints.	
End point type	Secondary
End point timeframe:	
Blood samples were collected at baseline and after 180 minutes post-medication.	

End point values	Tadalafil - baseline	Tadalafil - 180 minutes	Placebo - baseline	Placebo - 180 minutes
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	19	20	20
Units: pg/ml				
arithmetic mean (standard deviation)	4619.2 (± 207.2)	4764.5 (± 2566.5)	4836.1 (± 2383.2)	4489.6 (± 2938.2)

Statistical analyses

Statistical analysis title	T-test
Statistical analysis description:	
Total number of subjects: 19 in tadalafil and 20 in placebo.	

Comparison groups	Tadalafil - baseline v Tadalafil - 180 minutes v Placebo - baseline v Placebo - 180 minutes
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	other[13]
P-value	< 0.05
Method	t-test, 2-sided

Notes:

[13] - We performed a paired sample T-test.

Secondary: Blood sample - TNF-alpha

End point title	Blood sample - TNF-alpha

End point description:

Changes in biomarker concentration before and after tadalafil/placebo for each subject were calculated and then further used for statistical analysis. Here, results are shown as the mean value and standard deviation for both groups at the different timepoints.

End point type	Secondary

End point timeframe:

Blood samples were collected at baseline and after 180 minutes post-medication.

End point values	Tadalafil - baseline	Tadalafil - 180 minutes	Placebo - baseline	Placebo - 180 minutes
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	19	20	20
Units: pg/ml				
arithmetic mean (standard deviation)	2.13 (± 0.72)	2.05 (± 0.85)	2.12 (± 0.90)	2.52 (± 1.76)

Statistical analyses

Statistical analysis title	T-test

Statistical analysis description:

Total number of subjects: 19 in tadalafil and 20 in placebo.

Comparison groups	Tadalafil - baseline v Tadalafil - 180 minutes v Placebo - baseline v Placebo - 180 minutes
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	other[14]
P-value	< 0.05
Method	t-test, 2-sided

Notes:

[14] - We performed a paired sample T-test.

Secondary: Blood sample - IL-6

End point title	Blood sample - IL-6

End point description:

Changes in biomarker concentration before and after tadalafil/placebo for each subject were calculated and then further used for statistical analysis. Here, results are shown as the mean value and standard

deviation for both groups at the different timepoints.

End point type	Secondary

End point timeframe:

Blood samples were collected at baseline and after 180 minutes post-medication.

End point values	Tadalafil - baseline	Tadalafil - 180 minutes	Placebo - baseline	Placebo - 180 minutes
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	19	20	20
Units: pg/ml				
arithmetic mean (standard deviation)	0.94 (± 0.38)	2.21 (± 3.35)	1.05 (± 0.55)	4.52 (± 7.95)

Statistical analyses

Statistical analysis title	T-test

Statistical analysis description:

Total number of subjects: 19 in tadalafil and 20 in placebo.

Comparison groups	Tadalafil - baseline v Tadalafil - 180 minutes v Placebo - baseline v Placebo - 180 minutes
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	other[15]
P-value	< 0.05
Method	t-test, 2-sided

Notes:

[15] - We performed a paired sample T-test.

Secondary: Blood sample - IL1-beta

End point title	Blood sample - IL1-beta

End point description:

Changes in biomarker concentration before and after tadalafil/placebo for each subject were calculated and then further used for statistical analysis. Here, results are shown as the mean value and standard deviation for both groups at the different timepoints.

End point type	Secondary

End point timeframe:

Blood samples were collected at baseline and after 180 minutes post-medication.

End point values	Tadalafil - baseline	Tadalafil - 180 minutes	Placebo - baseline	Placebo - 180 minutes
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	19	20	20
Units: pg/ml				
arithmetic mean (standard deviation)	0.16 (± 0.12)	0.04 (± 0.02)	0.10 (± 0.06)	0.20 (± 0.11)

Statistical analyses

Statistical analysis title	T-test

Statistical analysis description:

Total number of subjects: 19 in tadalafil and 20 in placebo.

Comparison groups	Tadalafil - baseline v Tadalafil - 180 minutes v Placebo - baseline v Placebo - 180 minutes
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	other[16]
P-value	< 0.05
Method	t-test, 2-sided

Notes:

[16] - We performed a paired sample T-test.

Secondary: Blood sample - VCAM1

End point title	Blood sample - VCAM1

End point description:

Changes in biomarker concentration before and after tadalafil/placebo for each subject were calculated and then further used for statistical analysis. Here, results are shown as the mean value and standard deviation for both groups at the different timepoints.

End point type	Secondary

End point timeframe:

Blood samples were collected at baseline and after 180 minutes post-medication.

End point values	Tadalafil - baseline	Tadalafil - 180 minutes	Placebo - baseline	Placebo - 180 minutes
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	19	20	20
Units: pg/ml				
arithmetic mean (standard deviation)	624348.39 (± 231467.28)	797138.04 (± 245361.56)	777176.51 (± 297499.83)	718597.67 (± 379344.50)

Statistical analyses

Statistical analysis title	T-test

Statistical analysis description:

Total number of subjects: 19 in tadalafil and 20 in placebo.

Comparison groups	Tadalafil - baseline v Tadalafil - 180 minutes v Placebo - baseline v Placebo - 180 minutes

Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	other[17]
P-value	< 0.05
Method	t-test, 2-sided

Notes:

[17] - We performed a paired sample T-test.

Secondary: Blood sample - ICAM1

End point title	Blood sample - ICAM1

End point description:

Changes in biomarker concentration before and after tadalafil/placebo for each subject were calculated and then further used for statistical analysis. Here, results are shown as the mean value and standard deviation for both groups at the different timepoints.

End point type	Secondary

End point timeframe:

Blood samples were collected at baseline and after 180 minutes post-medication.

End point values	Tadalafil - baseline	Tadalafil - 180 minutes	Placebo - baseline	Placebo - 180 minutes
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	19	20	20
Units: pg/ml				
arithmetic mean (standard deviation)	354852.44 (± 154885.50)	476033.98 (± 169334.63)	459055.08 (± 195422.13)	402261.70 (± 190472.98)

Statistical analyses

Statistical analysis title	T-test

Statistical analysis description:

Total number of subjects: 19 in tadalafil and 20 in placebo.

Comparison groups	Tadalafil - 180 minutes v Placebo - baseline v Placebo - 180 minutes v Tadalafil - baseline
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	other[18]
P-value	< 0.05
Method	t-test, 2-sided

Notes:

[18] - We performed a paired sample T-test.

Secondary: Blood sample - VEGF

End point title	Blood sample - VEGF

End point description:

Changes in biomarker concentration before and after tadalafil/placebo for each subject were calculated and then further used for statistical analysis. Here, results are shown as the mean value and standard deviation for both groups at the different timepoints.

End point type	Secondary

End point timeframe:

Blood samples were collected at baseline and after 180 minutes post-medication.

End point values	Tadalafil - baseline	Tadalafil - 180 minutes	Placebo - baseline	Placebo - 180 minutes
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	19	20	20
Units: pg/ml				
arithmetic mean (standard deviation)	21.88 (± 8.24)	26.927 (± 8.85)	23.82 (± 9.99)	30.14 (± 8.39)

Statistical analyses

Statistical analysis title	T-test

Statistical analysis description:

Total number of subjects: 19 in tadalafil and 20 in placebo.

Comparison groups	Tadalafil - baseline v Tadalafil - 180 minutes v Placebo - baseline v Placebo - 180 minutes
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	other[19]
P-value	< 0.05
Method	t-test, 2-sided

Notes:

[19] - We performed a paired sample T-test.

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
During the whole trial period.	
Adverse event reporting additional description:	
Questionare given to the subjects. Subjects were asked to note all adverse events for three days after the trial days.	
Assessment type	Systematic

Dictionary used	
Dictionary name	Events not coded
Dictionary version	N/A

Reporting groups	
Reporting group title	Tadalafil
Reporting group description:	
Crossover trial. Tadalafil (20 mg) was given as a single dose during trial day one or two. Placebo was given on the other trial day.	
Reporting group title	Placebo
Reporting group description:	
Crossover trial. Placebo was given as a single dose during trial day one or two. Tadalafil was given on the other trial day.	

Serious adverse events	Tadalafil	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Tadalafil	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 19 (26.32%)	6 / 20 (30.00%)	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 19 (10.53%)	1 / 20 (5.00%)	
occurrences (all)	2	1	
Ear and labyrinth disorders			
Dizziness			

subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Social circumstances			
Sleep deficit			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 19 (5.26%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Fatigue			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 19 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	

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