



Clinical trial results:

Use of doxapram as a new antiarrhythmic drug for a specific therapy of atrial fibrillation Doctos Trial (Doxapram conversion to sinus rhythm study)

Summary

EudraCT number	2018-002979-17
Trial protocol	DE
Global end of trial date	25 October 2023

Results information

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

Trial information

Trial identification

Sponsor protocol code	K620
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University of Heidelberg
Sponsor organisation address	Im Neuenheimer Feld 410, Heidelberg, Germany, 69120
Public contact	Department of Clinical Pharmacology, University of Heidelberg, 0049 6221568740, Walter.Emil.Haefeli@med.uni-heidelberg.de
Scientific contact	Department of Clinical Pharmacology, University of Heidelberg, 0049 6221568740, Walter.Emil.Haefeli@med.uni-heidelberg.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	13 August 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 October 2023
Global end of trial reached?	Yes
Global end of trial date	25 October 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Antiarrhythmic potential for cardioversion from AF to SR after i.v. administration of doxapram

Protection of trial subjects:

All drug used in this trial are approved in Germany and have a well-known side effect and acceptable safety profile.

For all PK parameters, blood samples were taken from a peripheral venous catheter. This procedure is generally well tolerated.

During the study, Patient's health was closely monitored during the trial. Precautions were taken to discover

and treat any adverse events early and appropriately. (S)AEs including SUSARs were reported.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 January 2019
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: 23
Worldwide total number of subjects	23
EEA total number of subjects	23

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	15

85 years and over	0
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Subject disposition

Recruitment

Recruitment details:

in-house patients suffering from Paroxysmal or persistent, non-valvular, atrial fibrillation (AF) meeting eligibility criteria for non-emergent, electrical or pharmacological cardioversion were included

Pre-assignment

Screening details:

right before treatment: Inclusion, exclusion criteria were checked; relevant medical history, current medical condition were assessed. Complete physical examination, urine and blood analysis, ECG were conducted. Abnormal parameters may re-tested. Last value obtained defined eligibility.

Period 1

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

Blinding implementation details:

not necessary

Arms

Are arms mutually exclusive?	Yes
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Arm title	Cohort 1
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Arm description:

2 x bolus of 0.5 mg/kg body weight IMP for conversion

Arm type	Experimental
Investigational medicinal product name	Doxapram hydrochloride
Investigational medicinal product code	6743066.00.00
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

up to 2 identical doses, given as bolus, at least 20 min apart

Arm title	Cohort 2
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Arm description:

2 x 1 mg/kg body weight

Arm type	Experimental
Investigational medicinal product name	Doxapram hydrochloride
Investigational medicinal product code	6743066.00.00
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

up to 2 identical doses, given as bolus, at least 20 min apart

Arm title	Cohort 3
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Arm description:

2 x 2 mg/kg body weight

Arm type	Experimental
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Investigational medicinal product name	Doxapram hydrochloride
Investigational medicinal product code	6743066.00.00
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

up to 2 identical doses, given as bolus, at least 20 min apart

Arm title	Cohort 4
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Arm description:

8 mg/kg body weight, infusion over 8 h

Arm type	Experimental
Investigational medicinal product name	Doxapram hydrochloride
Investigational medicinal product code	6743066.00.00
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Continuous i. v. infusion over 8 h. Infusion was allowed to be interrupted and/or infusion time prolonged if required to limit blood pressure increase

Number of subjects in period 1	Cohort 1	Cohort 2	Cohort 3
Started	7	6	6
Completed	7	6	6

Number of subjects in period 1	Cohort 4
Started	4
Completed	4

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1
Reporting group description: 2 x bolus of 0.5 mg/kg body weight IMP for conversion	
Reporting group title	Cohort 2
Reporting group description: 2 x 1 mg/kg body weight	
Reporting group title	Cohort 3
Reporting group description: 2 x 2 mg/kg body weight	
Reporting group title	Cohort 4
Reporting group description: 8 mg/kg body weight, infusion over 8 h	

Reporting group values	Cohort 1	Cohort 2	Cohort 3
Number of subjects	7	6	6
Age categorical Units: Subjects			
Adults (18-64 years)	2	2	3
From 65-84 years	5	4	3
Gender categorical Units: Subjects			
Female	1	1	4
Male	6	5	2

Reporting group values	Cohort 4	Total	
Number of subjects	4	23	
Age categorical Units: Subjects			
Adults (18-64 years)	1	8	
From 65-84 years	3	15	
Gender categorical Units: Subjects			
Female	0	6	
Male	4	17	

End points

End points reporting groups

Reporting group title	Cohort 1
Reporting group description: 2 x bolus of 0.5 mg/kg body weight IMP for conversion	
Reporting group title	Cohort 2
Reporting group description: 2 x 1 mg/kg body weight	
Reporting group title	Cohort 3
Reporting group description: 2 x 2 mg/kg body weight	
Reporting group title	Cohort 4
Reporting group description: 8 mg/kg body weight, infusion over 8 h	

Primary: Rate of cardioversion from AF to SR after i. v. administration of doxapram.

End point title	Rate of cardioversion from AF to SR after i. v. administration of doxapram. ^[1]
End point description: measured by 12-lead ECG	
End point type	Primary
End point timeframe: within 6 h after i. v. doxapram	

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: not enough data available to meet criteria for statistical analysis

End point values	Cohort 1	Cohort 2	Cohort 3	Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	6	4
Units: cardioversion	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: time to cardioversion from AF to SR after i. v. administration of doxapram

End point title	time to cardioversion from AF to SR after i. v. administration of doxapram
End point description:	
End point type	Secondary

End point timeframe:
from start of treatment to end of study

End point values	Cohort 1	Cohort 2	Cohort 3	Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	6	4
Units: time				
arithmetic mean (full range (min-max))	10.15 (6.87 to 13.42)	0 (0 to 0)	0 (0 to 0)	16.1 (06.25 to 23.05)

Statistical analyses

No statistical analyses for this end point

Secondary: SR after pharmacological or electrical cardioversion at day 7

End point title	SR after pharmacological or electrical cardioversion at day 7
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End point description:

End point type	Secondary
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End point timeframe:

7 +/- 2 days after doxapram exposure

End point values	Cohort 1	Cohort 2	Cohort 3	Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	4
Units: sinus rhythm	6	6	6	3

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The observation period begins with the first administration of the IMP (any adverse events prior to the first administration of the IMP are documented as medical history) and ends after 7 ± 2 days.

Assessment type	Systematic
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Dictionary used

Dictionary name	CTCAE
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Dictionary version	5
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Reporting groups

Reporting group title	Treatment to EOS
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Reporting group description: -

Serious adverse events	Treatment to EOS		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 23 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Treatment to EOS		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 23 (100.00%)		
Cardiac disorders			
palpitation			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
sinusbradycardia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Nervous system disorders			
headache			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	3		
tremor			

subjects affected / exposed occurrences (all) paresthesia (hands) subjects affected / exposed occurrences (all) nightly confusion subjects affected / exposed occurrences (all)	10 / 23 (43.48%) 10 1 / 23 (4.35%) 1 1 / 23 (4.35%) 1		
General disorders and administration site conditions feeling of warmth subjects affected / exposed occurrences (all) preasure feeling head subjects affected / exposed occurrences (all)	23 / 23 (100.00%) 26 2 / 23 (8.70%) 2		
Ear and labyrinth disorders dizziness subjects affected / exposed occurrences (all) tinnitus subjects affected / exposed occurrences (all)	11 / 23 (47.83%) 11 2 / 23 (8.70%) 2		
Gastrointestinal disorders nausea subjects affected / exposed occurrences (all) dry mouth subjects affected / exposed occurrences (all)	2 / 23 (8.70%) 2 1 / 23 (4.35%) 1		
Respiratory, thoracic and mediastinal disorders altered breathing subjects affected / exposed occurrences (all) Chest pain subjects affected / exposed occurrences (all)	12 / 23 (52.17%) 12 2 / 23 (8.70%) 2		

Skin and subcutaneous tissue disorders rash subjects affected / exposed occurrences (all) sweating subjects affected / exposed occurrences (all) tingeling both upper legs subjects affected / exposed occurrences (all)	1 / 23 (4.35%) 1 1 / 23 (4.35%) 1 1 / 23 (4.35%) 1		
Endocrine disorders latent hyperhyreosis subjects affected / exposed occurrences (all)	1 / 23 (4.35%) 1		
Musculoskeletal and connective tissue disorders muscle fasciculations (wohle body) subjects affected / exposed occurrences (all)	1 / 23 (4.35%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 August 2019	Adjustment of: inclusion criteria, exclusion criteria, Dose escalation and dose deescalation, pregnancy prevention requirements
29 April 2020	Additional cohort, updated timelines, tighten blood pressure control, add exploratory evaluation of catecholamines during elevated blood pressure
09 June 2022	changes in: - safety or integrity of trial subjects - conduct or management of the trial - or addition of principal investigator(s), co-ordinating investigator

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported