



Clinical trial results:

Pharmacokinetics of edoxaban in geriatric patients with atrial fibrillation Summary

EudraCT number	2022-004136-26
Trial protocol	BE
Global end of trial date	24 April 2024

Results information

Result version number	v1 (current)
This version publication date	08 May 2025
First version publication date	08 May 2025
Summary attachment (see zip file)	Summary (Summary - PK of edoxaban.docx)

Trial information

Trial identification

Sponsor protocol code	S67063
-----------------------	--------

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	UZ Leuven
Sponsor organisation address	UZ Herestraat 49, Leuven, Belgium, 3000
Public contact	Clinical Trial Center, UZ Leuven, 00 3216 34 19 98, ctc@uzleuven.be
Scientific contact	Clinical Trial Center, UZ Leuven, 00 3216 34 19 98, ctc@uzleuven.be

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	15 October 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	24 April 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To explore the pharmacokinetics (PK) of edoxaban in a special patient population of geriatric inpatients with atrial fibrillation

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. Ethical approval was obtained from the relevant Ethics Committee prior to study initiation. All participants or their legally authorized representatives provided written informed consent after receiving both verbal and written information about the study's purpose, procedures, risks, and benefits.

Special attention was given to the vulnerability of the geriatric population, including assessment of their capacity to consent and close monitoring for adverse events. To minimize participant burden, a peripheral venous catheter was used for serial blood sampling, reducing the discomfort and risk associated with multiple venipunctures. Additionally, visits were scheduled to accommodate participants' needs, and the number of blood samples was limited to what was essential for reliable pharmacokinetic analysis.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2023
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	Belgium: 17
Worldwide total number of subjects	17
EEA total number of subjects	17

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)	0
From 65 to 84 years	5
85 years and over	12

Subject disposition

Recruitment

Recruitment details:

Start date of the recruitment: 1 September 2023

The last patient visit: 24 April 2024

All recruitment was conducted in the UZ Leuven, Belgium.

Pre-assignment

Screening details:

inclusion criteria:

- Patients aged at least 75 years who are currently admitted to one of the geriatric wards
- with atrial fibrillation and on edoxaban dose 30 or 60 mg
- no anemia and clinically stable

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:

Blinding method is not applicable as it is a pharmacokinetics study

Arms

Arm title	overall
-----------	---------

Arm description:

division into arms is not applicable as it is an observational pharmacokinetics study when all subjects received edoxaban and contributed to blood samples

Arm type	Experimental
Investigational medicinal product name	Edoxaban
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

30 and 60 mg

Number of subjects in period 1	overall
Started	17
Completed	17

Baseline characteristics

Reporting groups

Reporting group title	overall trial
-----------------------	---------------

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	17	17	
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)	0	0	
From 65-84 years	5	5	
85 years and over	12	12	
Age continuous			
Units: years			
median	87		
inter-quartile range (Q1-Q3)	83 to 90	-	
Gender categorical			
Units: Subjects			
Female	7	7	
Male	10	10	

End points

End points reporting groups

Reporting group title	overall
Reporting group description: division into arms is not applicable as it is an observational pharmacokinetics study when all subjects received edoxaban and contributed to blood samples	
Subject analysis set title	Subjects with PPI
Subject analysis set type	Full analysis
Subject analysis set description: Subset of the dataset which contains subjects co-medicated with proton pump inhibitor drugs	
Subject analysis set title	Subjects without PPI
Subject analysis set type	Full analysis
Subject analysis set description: Subset of the dataset which contains subjects who were not co-medicated with proton pump inhibitor drugs	

Primary: Clearance

End point title	Clearance
End point description: Edoxaban concentrations at these time points: pre-dose, 0.5, 1, 1.5, 2, 4, 5, 8 hours after dose, were used to build a population pharmacokinetics model that estimates edoxaban clearance in geriatric patients.	
End point type	Primary
End point timeframe: 0 until 24 hours after the dose	

End point values	Subjects with PPI	Subjects without PPI		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	7		
Units: L/h				
median (confidence interval 95%)	11.8 (11.7 to 12.1)	9.01 (8.9 to 9.2)		

Statistical analyses

Statistical analysis title	Population pharmacokinetics analysis
Statistical analysis description: Edoxaban concentrations at these time points: pre-dose, 0.5, 1, 1.5, 2, 4, 5, 8 hours after dose, were used to build a population pharmacokinetics model that estimates edoxaban clearance in geriatric patients.	
Comparison groups	Subjects with PPI v Subjects without PPI

Number of subjects included in analysis	17
Analysis specification	Post-hoc
Analysis type	other ^[1]
P-value	< 0.01
Method	non-linear mixed model

Notes:

[1] - In this exploratory population pharmacokinetics analysis/modeling, no comparison groups were pre-specified. The categorization of groups with PPI and without PPI was based on the significance in the exploration of the important covariates.

Primary: Volume of distribution

End point title	Volume of distribution
-----------------	------------------------

End point description:

End point type	Primary
----------------	---------

End point timeframe:

0 until 24 hours after the dose

End point values	Subjects with PPI	Subjects without PPI		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	7		
Units: L				
median (confidence interval 95%)	62.6 (53.02 to 72.6)	47.6 (40.3 to 55.2)		

Statistical analyses

Statistical analysis title	Population pharmacokinetics analysis
----------------------------	--------------------------------------

Statistical analysis description:

Edoxaban concentrations at these time points: pre-dose, 0.5, 1, 1.5, 2, 4, 5, 8 hours after dose, were used to build a population pharmacokinetics model that estimates edoxaban volume of distribution in geriatric patients.

Comparison groups	Subjects without PPI v Subjects with PPI
Number of subjects included in analysis	17
Analysis specification	Post-hoc
Analysis type	other ^[2]
P-value	< 0.01
Method	non-linear mixed model

Notes:

[2] - In this exploratory population pharmacokinetics analysis/modeling, no comparison groups were pre-specified. The categorization of groups with PPI and without PPI was based on the significance in the exploration of the important covariates.

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

1 September 2023 - 24 April 2024

Assessment type	Non-systematic
-----------------	----------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	24.0
--------------------	------

Reporting groups

Reporting group title	Overall
-----------------------	---------

Reporting group description: -

Serious adverse events	Overall		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 17 (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	Overall		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 17 (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: This is an observational pharmacokinetics study which we only included those patients already received edoxaban routinely and collected their blood samples using catheter, so the adverse event related to this study was none.

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

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

We expected to include 30 subjects; however, because of limited time and budget, we did not extend the study period. As a results, only 17 subjects were included and analyzed.

Notes: