Clinical trial results:
Pulmonary vein isolation with versus without continued antiarrhythmic drug treatment in subjects with persistent atrial fibrillation: a prospective multi-centre randomized controlled clinical study (POWDER-AF2 study)

Summary

EudraCT number	2018-002103-33
Trial protocol	AT DK ES FR
Global end of trial date	01 August 2023

Results information

Result version number	v1 (current)
This version publication date	17 December 2023
First version publication date	17 December 2023
Summary attachment (see zip file)	Published Study Paper (demolder-et-al-2023-no-effect-of-continued-antiarrhythmic-drug-treatment-on-top-of-optimized-pulmonary-vein-isolation (1).pdf)

Trial information

Trial identification

Sponsor protocol code	1080719

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	ClinicalTrials.gov: NCT03437356

Notes:

Sponsors

Sponsor organisation name	AZ Sint-Jan Brugge-Oostende AV
Sponsor organisation address	Ruddershove 10, Bruges, Belgium,
Public contact	Anthony Demolder, Anthony Demolder, anthony.demolder@ugent.be
Scientific contact	Anthony Demolder, Anthony Demolder, anthony.demolder@ugent.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	01 August 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 August 2023
Global end of trial reached?	Yes
Global end of trial date	01 August 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

We aimed to study whether continued ADT (antiarrhythmic drug treatment) (ADT ON) beyond the 3 month blanking period reduces recurrrence of atrial tachyarrhyhtmia (ATA) in the first year after contact-force guided pulmonary vein isolation (PVI) for persistent AF.

Protection of trial subjects:

As per standard follow-up.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 June 2018
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	Spain: 17
Country: Number of subjects enrolled	Austria: 36
Country: Number of subjects enrolled	Denmark: 11
Country: Number of subjects enrolled	Belgium: 117
Country: Number of subjects enrolled	Switzerland: 19
Worldwide total number of subjects	200
EEA total number of subjects	181

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)	20

From 65 to 84 years	180
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients planned for first-time ablation of PersAF (defined as any prior episode ≥7 days)8 were locally screened for inclusion. Inclusion criteria were symptomatic PersAF resistant to ongoing or prior ADT (failed class IC or III ADT) and at least 1 episode of PersAF in the last year.

Period 1

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

Blinding implementation details:

At the time of procedural planning, enrolled patients were randomly assigned (block randomization with center stratification) to continue (ADT ON group) or discontinue previously ineffective ADT (ADT OFF group) after the 3-month blanking period up to 1 year after ablation. In the ADT ON group, ADT was continued after verifying for correct dosage according to the European Society of Cardiology guidelines on the treatment of AF.

Arms

Are arms mutually exclusive?	Yes
Arm title	ADT ON

Arm description:

In the ADT ON group, ADT was continued after verifying for correct dosage according to the European Society of Cardiology guidelines on the treatment of AF. If not already the case, β-blocking agents were added to Class 1C ADT. In the case of preprocedural use of amiodarone, ADT was switched to conventional class 1C or sotalol. In the ADT OFF group, all antiarrhythmic medications were discontinued after the 3-month blanking period with the exception of β-blocking agents if these were given for other indications (eg, hypertension, ischemic heart disease).

Arm type	Active comparator
Investigational medicinal product name	Class 1C antiarrhythmic drugs
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

According to the Summary of Product Characteristics (SmPC) and in line with physician instructions.

Arm title	ADT OFF

Arm description:

At the time of procedural planning, enrolled patients were randomly assigned (block randomization with center stratification) to continue (ADT ON group) or discontinue previously ineffective ADT (ADT OFF group) after the 3-month blanking period up to 1 year after ablation. In the ADT OFF group, all antiarrhythmic medications were discontinued after the 3-month blanking period with the exception of β-blocking agents if these were given for other indications (eg, hypertension, ischemic heart disease).

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	ADT ON	ADT OFF
Started	102	98
Completed	99	95
Not completed	3	3
Lost to follow-up	3	3

Baseline characteristics

Reporting groups	
Reporting group title	ADT ON

Reporting group description:

In the ADT ON group, ADT was continued after verifying for correct dosage according to the European Society of Cardiology guidelines on the treatment of AF. If not already the case, β-blocking agents were added to Class 1C ADT. In the case of preprocedural use of amiodarone, ADT was switched to conventional class 1C or sotalol. In the ADT OFF group, all antiarrhythmic medications were discontinued after the 3-month blanking period with the exception of β-blocking agents if these were given for other indications (eg, hypertension, ischemic heart disease).

Reporting group title	ADT OFF

Reporting group description:

At the time of procedural planning, enrolled patients were randomly assigned (block randomization with center stratification) to continue (ADT ON group) or discontinue previously ineffective ADT (ADT OFF group) after the 3-month blanking period up to 1 year after ablation. In the ADT OFF group, all antiarrhythmic medications were discontinued after the 3-month blanking period with the exception of β-blocking agents if these were given for other indications (eg, hypertension, ischemic heart disease).

Reporting group values	ADT ON	ADT OFF	Total
Number of subjects	102	98	200
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	65	65	
standard deviation	± 8	± 9	-
Gender categorical Units: Subjects			
Female	29	32	61
Male	73	66	139

End points

End points reporting groups

Reporting group title	ADT ON

Reporting group description:

In the ADT ON group, ADT was continued after verifying for correct dosage according to the European Society of Cardiology guidelines on the treatment of AF. If not already the case, β-blocking agents were added to Class 1C ADT. In the case of preprocedural use of amiodarone, ADT was switched to conventional class 1C or sotalol. In the ADT OFF group, all antiarrhythmic medications were discontinued after the 3-month blanking period with the exception of β-blocking agents if these were given for other indications (eg, hypertension, ischemic heart disease).

Reporting group title	ADT OFF

Reporting group description:

At the time of procedural planning, enrolled patients were randomly assigned (block randomization with center stratification) to continue (ADT ON group) or discontinue previously ineffective ADT (ADT OFF group) after the 3-month blanking period up to 1 year after ablation. In the ADT OFF group, all antiarrhythmic medications were discontinued after the 3-month blanking period with the exception of β-blocking agents if these were given for other indications (eg, hypertension, ischemic heart disease).

Subject analysis set title	Analysis of primary endpoint
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Except for the Kaplan-Meier survival curve and the Cox regression model, the analysis was performed in accordance to the modified intention-to-treat principle excluding patients who were lost to follow-up or died before completing the 12-month follow-up visit. Statistical tests were 2-tailed, and P≤0.05 was considered statistically significant. Analyses were conducted using SPSS, version 28.0 (IBM Corporation, Armonk, NY).

Primary: Any documented ATA (AF, atrial flutter, or atrial tachycardia) lasting >30 seconds between 3 and 12 months of follow-up

End point title	Any documented ATA (AF, atrial flutter, or atrial tachycardia) lasting >30 seconds between 3 and 12 months of follow-up

End point description:

End point type	Primary

End point timeframe:

Between 3 and 12 months follow-up.

End point values	ADT ON	ADT OFF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	98		
Units: Count (n, %)	21	19		

Attachments (see zip file)	demolder-et-al-2023-no-effect-of-continued-antiarrhythmic-

Statistical analyses

Statistical analysis title	Kaplan Meier analysis
Comparison groups	ADT ON v ADT OFF

Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.797
Method	Logrank

Secondary: Number of repeat ablations

End point title	Number of repeat ablations

End point description:

End point type	Secondary

End point timeframe:

Between 3 and 12 months follow-up.

End point values	ADT ON	ADT OFF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	98		
Units: Count (n, %)	6	11		

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Statistical analyses

Statistical analysis title	Kaplan Meier analysis
Comparison groups	ADT OFF v ADT ON
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.127
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.17
upper limit	1.25

Secondary: Number of unscheduled arrhythmia-related health care provider visits

End point title	Number of unscheduled arrhythmia-related health care provider visits

End point description:

End point type	Secondary

End point timeframe:

3 months until 12 months follow-up.

End point values	ADT ON	ADT OFF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	98		
Units: Count (n, %)	14	18		

Statistical analyses

Statistical analysis title	Kaplan Meier analysis
Comparison groups	ADT ON v ADT OFF
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.399
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	1.49

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From baseline until 12 month follow-up.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups	
Reporting group title	ADT ON

Reporting group description:

In the ADT ON group, ADT was continued after verifying for correct dosage according to the European Society of Cardiology guidelines on the treatment of AF. If not already the case, β-blocking agents were added to Class 1C ADT. In the case of preprocedural use of amiodarone, ADT was switched to conventional class 1C or sotalol. In the ADT OFF group, all antiarrhythmic medications were discontinued after the 3-month blanking period with the exception of β-blocking agents if these were given for other indications (eg, hypertension, ischemic heart disease).

Serious adverse events	ADT ON		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 102 (0.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	ADT ON		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 102 (8.82%)		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	2 / 102 (1.96%)		
occurrences (all)	2		
Exercise tolerance decreased			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	3 / 102 (2.94%)		
occurrences (all)	3		
Other adverse events suspected by patients	Additional description: Other adverse events suspected by patients but without clinical evidence.		
subjects affected / exposed	3 / 102 (2.94%)		
occurrences (all)	3		

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/37921006