



Clinical trial results:

A Phase 2, Multi-Center, Randomized, Double-Blind, Placebo-Controlled, Dose Ranging Study to Evaluate the Efficacy and Safety of Botulinum Toxin Type A (AGN-151607) Injections into the Epicardial Fat Pads to Prevent Post-Operative Atrial Fibrillation in Patients Undergoing Open-Chest Cardiac Surgery

Summary

EudraCT number	2017-004399-68
Trial protocol	GB DE ES AT SE NL IT
Global end of trial date	06 March 2023

Results information

Result version number	v2 (current)
This version publication date	16 June 2024
First version publication date	20 March 2024
Version creation reason	<ul style="list-style-type: none">• Correction of full data set Edits made to clarify text and clarify data table in 1 secondary endpoint.

Trial information

Trial identification

Sponsor protocol code	1925-201-008
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03779841
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co. KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6 4UB
Public contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com

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	06 March 2023
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	06 March 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This was a multi-center, randomized, double-blind, placebo-controlled, parallel group, dose-ranging study to evaluate the efficacy and safety of botulinum toxin type A (AGN-151607) injections into the epicardial fat pads, foci of ganglionic plexi, to prevent Post-Operative Atrial Fibrillation (POAF) in patients undergoing open-chest cardiac surgery.

Protection of trial subjects:

Prior to the initiation of any screening or study-specific procedures, the investigator or his or her representative explained the nature of the study to the subject or his or her representative and answered all questions regarding this study. The informed consent statement was reviewed and signed and dated by the subject and the person who administered the informed consent. A copy of the signed informed consent was to be given to the subject and the original was to be placed in the subject's medical record.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 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	United Kingdom: 5
Country: Number of subjects enrolled	United States: 186
Country: Number of subjects enrolled	Austria: 4
Country: Number of subjects enrolled	Canada: 97
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	Sweden: 3
Worldwide total number of subjects	319
EEA total number of subjects	31

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)	130
From 65 to 84 years	189
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 323 subjects were randomized, of which 319 received study drug (Safety Population).

Period 1

Period 1 title	Overall Study Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Injections of placebo were made into each 1 of 5 fat pads. The total injection volume into each fat pad was 1mL. One-time treatment.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Other use

Dosage and administration details:

The placebo solution for injection contained only the excipients of AGN-151607. Subjects received a single dose divided into five equal injections to be administered into five epicardial fat pads during the open-chest surgery.

Arm title	AGN-151607 (125 U)
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Arm description:

Injections of 25 U were made into each 1 of 5 fat pads. The total injection volume into each fat pad was 1 mL. One-time treatment.

Arm type	Experimental
Investigational medicinal product name	Clostridium botulinum toxin type A
Investigational medicinal product code	AGN-151607
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Other use

Dosage and administration details:

A lyophilized formulation consisting of AGN-151607 was reconstituted. Subjects received a single dose divided into five equal injections to be administered into five epicardial fat pads during the open-chest surgery for total dose of 125 U.

Arm title	AGN-151607 (250 U)
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Arm description:

Injections of 50 U were made into each 1 of 5 fat pads. The total injection volume into each fat pad was 1 mL. One-time treatment.

Arm type	Experimental
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Investigational medicinal product name	Clostridium botulinum toxin type A
Investigational medicinal product code	AGN-151607
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Other use

Dosage and administration details:

A lyophilized formulation consisting of AGN-151607 was reconstituted. Subjects received a single dose divided into five equal injections to be administered into five epicardial fat pads during the open-chest surgery for total dose of 250 U.

Number of subjects in period 1	Placebo	AGN-151607 (125 U)	AGN-151607 (250 U)
Started	105	105	109
Completed	94	87	93
Not completed	11	18	16
Adverse event, serious fatal	1	-	2
Consent withdrawn by subject	4	8	6
Adverse event, non-fatal	1	1	-
Lost to follow-up	5	9	8

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description: Injections of placebo were made into each 1 of 5 fat pads. The total injection volume into each fat pad was 1mL. One-time treatment.	
Reporting group title	AGN-151607 (125 U)
Reporting group description: Injections of 25 U were made into each 1 of 5 fat pads. The total injection volume into each fat pad was 1 mL. One-time treatment.	
Reporting group title	AGN-151607 (250 U)
Reporting group description: Injections of 50 U were made into each 1 of 5 fat pads. The total injection volume into each fat pad was 1 mL. One-time treatment.	

Reporting group values	Placebo	AGN-151607 (125 U)	AGN-151607 (250 U)
Number of subjects	105	105	109
Age categorical Units: Subjects			
Between 18 and 64 years	43	42	45
≥ 65 years	62	63	64
Age continuous Units: years			
arithmetic mean	66.8	66.8	67.2
standard deviation	± 6.76	± 6.54	± 7.01
Gender categorical Units: Subjects			
Female	14	17	22
Male	91	88	87
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	6	8	6
Not Hispanic or Latino	99	97	103
Race (NIH/OMB) Units: Subjects			
Asian	1	0	2
Black or African American	2	2	2
White	102	102	105
Unknown or Not Reported	0	1	0
Type of Surgery			
CABG = Coronary Artery Bypass Graft			
Units: Subjects			
Isolated CABG Surgery	65	68	70
Valve only Surgery	27	24	27
CABG and Valve Surgery	13	13	12

Reporting group values	Total		
Number of subjects	319		

Age categorical			
Units: Subjects			
Between 18 and 64 years	130		
≥ 65 years	189		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	53		
Male	266		
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	20		
Not Hispanic or Latino	299		
Race (NIH/OMB)			
Units: Subjects			
Asian	3		
Black or African American	6		
White	309		
Unknown or Not Reported	1		
Type of Surgery			
CABG = Coronary Artery Bypass Graft			
Units: Subjects			
Isolated CABG Surgery	203		
Valve only Surgery	78		
CABG and Valve Surgery	38		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Injections of placebo were made into each 1 of 5 fat pads. The total injection volume into each fat pad was 1mL. One-time treatment.	
Reporting group title	AGN-151607 (125 U)
Reporting group description: Injections of 25 U were made into each 1 of 5 fat pads. The total injection volume into each fat pad was 1 mL. One-time treatment.	
Reporting group title	AGN-151607 (250 U)
Reporting group description: Injections of 50 U were made into each 1 of 5 fat pads. The total injection volume into each fat pad was 1 mL. One-time treatment.	

Primary: Percentage of participants with at least 1 continuous AF (atrial fibrillation or atrial flutter) episode \geq 30 seconds during the first 30 days post-surgery

End point title	Percentage of participants with at least 1 continuous AF (atrial fibrillation or atrial flutter) episode \geq 30 seconds during the first 30 days post-surgery
End point description: At least one episode of continuous AF (atrial fibrillation or atrial flutter) sustained \geq 30 seconds documented by monitoring ECG measurements using ECG patches (ePatch) placed on the participant's chest. All randomized participants who received study treatment and had at least 1 post-dose ECG (by ePatch) by Day 30 post-surgery.	
End point type	Primary
End point timeframe: First 30 days following the initial intensive care unit (ICU) admission date after open-chest cardiac surgery.	

End point values	Placebo	AGN-151607 (125 U)	AGN-151607 (250 U)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	104	106	
Units: percentage of participants				
number (not applicable)	46.1	36.5	47.2	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).	
Comparison groups	AGN-151607 (125 U) v Placebo

Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1612
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	1.1

Statistical analysis title	Statistical Analysis 2
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Statistical analysis description:

P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).

Comparison groups	AGN-151607 (250 U) v Placebo
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7789
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.37

Secondary: Percentage of Time Spent in Atrial Fibrillation or Atrial Flutter (AF Burden) During the First 30 Days Post-surgery

End point title	Percentage of Time Spent in Atrial Fibrillation or Atrial Flutter (AF Burden) During the First 30 Days Post-surgery
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End point description:

The proportion of time an individual is in AF (atrial fibrillation or atrial flutter) during a monitoring period (expressed as a percentage) calculated as (the total time spent in AF during the first 30 days post-surgery divided by the total time of analyzable data obtained from the ECG patch during the first 30 days post-surgery) multiplied by 100. The calculation excludes continuous AF episodes < 30 seconds in duration.

All randomized participants who received study treatment and had at least 1 post-dose ECG (by ePatch) by Day 30 post-surgery.

End point type	Secondary
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End point timeframe:

First 30 days following the initial ICU admission date after open-chest cardiac surgery.

End point values	Placebo	AGN-151607 (125 U)	AGN-151607 (250 U)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	104	106	
Units: units on a scale				
arithmetic mean (standard deviation)	4.84 (± 14.898)	4.41 (± 14.976)	5.45 (± 15.821)	

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
P-value is obtained from stratified Wilcoxon (Van Elteren) test versus Placebo with type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years) as stratification factors.	
Comparison groups	AGN-151607 (250 U) v Placebo
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8722
Method	stratified Wilcoxon (Van Elteren)

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
P-value is obtained from stratified Wilcoxon (Van Elteren) test versus Placebo with type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years) as stratification factors.	
Comparison groups	AGN-151607 (125 U) v Placebo
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2972
Method	stratified Wilcoxon (Van Elteren)

Secondary: Percentage of Participants With at Least 1 Event of Symptomatic AF (Atrial Fibrillation or Atrial Flutter) During the First 30 Days Post-surgery

End point title	Percentage of Participants With at Least 1 Event of Symptomatic AF (Atrial Fibrillation or Atrial Flutter) During the First 30 Days Post-surgery
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End point description:

At least 1 event of symptomatic AF (atrial fibrillation or atrial flutter) (symptoms occurring within 2 hours of an AF episode). For symptomatic AF, symptoms that occur in the interval that starts two hours prior to the onset of the AF episode and ends two hours after the conclusion of the AF episode will meet the definition of "within 2 hours of an AF episode". AF episode ≥ 30 seconds.

All randomized participants who received study treatment and had at least 1 post-dose ECG (by ePatch)

by Day 30 post-surgery.

End point type	Secondary
End point timeframe:	
First 30 days following the initial ICU admission date after open-chest cardiac surgery.	

End point values	Placebo	AGN-151607 (125 U)	AGN-151607 (250 U)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	104	106	
Units: percentage of participants				
number (not applicable)	13.7	13.5	13.2	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).

Comparison groups	AGN-151607 (125 U) v Placebo
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9814
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1.96

Statistical analysis title	Statistical Analysis 2
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Statistical analysis description:

P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).

Comparison groups	AGN-151607 (250 U) v Placebo
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Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9715
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1.97

Secondary: Time to First Occurrence of AF (Atrial Fibrillation or Atrial Flutter) During the First 30 Days Post-surgery

End point title	Time to First Occurrence of AF (Atrial Fibrillation or Atrial Flutter) During the First 30 Days Post-surgery
End point description: Amount of time (days) to first AF (atrial fibrillation or atrial flutter) occurrence defined by first episode of AF lasting for ≥ 30 seconds.	
99999 = Insufficient number of participants with events	
End point type	Secondary
End point timeframe: First 30 days following the initial ICU admission date after open-chest cardiac surgery.	

End point values	Placebo	AGN-151607 (125 U)	AGN-151607 (250 U)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	104	106	
Units: days				
median (confidence interval 95%)	99999 (9.1 to 99999)	99999 (99999 to 99999)	99999 (13.2 to 99999)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: P-value is from stratified log-rank test versus Placebo with type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years) as stratification factors.	
Comparison groups	AGN-151607 (125 U) v Placebo

Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1281
Method	Logrank

Statistical analysis title	Statistical Analysis 2
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Statistical analysis description:

P-value is from stratified log-rank test versus Placebo with type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years) as stratification factors.

Comparison groups	AGN-151607 (250 U) v Placebo
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.882
Method	Logrank

Secondary: Percentage of Participants With at Least 1 Continuous AF (Atrial Fibrillation or Atrial Flutter) Episode ≥ 2 Minutes During the First 30 Days Post-surgery

End point title	Percentage of Participants With at Least 1 Continuous AF (Atrial Fibrillation or Atrial Flutter) Episode ≥ 2 Minutes During the First 30 Days Post-surgery
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End point description:

At least one episode of continuous AF (atrial fibrillation or atrial flutter) sustained ≥ 2 minutes documented by monitoring ECG measurements using ECG patches (ePatch) placed on the participant's chest.

All randomized participants who received study treatment and had at least 1 post-dose ECG (by ePatch) by Day 30 post-surgery.

End point type	Secondary
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End point timeframe:

First 30 days following the initial ICU admission date after open-chest cardiac surgery.

End point values	Placebo	AGN-151607 (125 U)	AGN-151607 (250 U)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	104	106	
Units: percentage of participants				
number (not applicable)	45.1	35.6	46.2	

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).	
Comparison groups	AGN-151607 (250 U) v Placebo
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7776
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.39

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).	
Comparison groups	AGN-151607 (125 U) v Placebo
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1623
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	1.1

Secondary: Percentage of Participants With at Least 1 Continuous AF (Atrial Fibrillation or Atrial Flutter) Episode ≥ 5 Minutes During the First 30 Days Post-surgery

End point title	Percentage of Participants With at Least 1 Continuous AF (Atrial Fibrillation or Atrial Flutter) Episode ≥ 5 Minutes During the First 30 Days Post-surgery
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End point description:

At least one episode of continuous AF (atrial fibrillation or atrial flutter) sustained ≥ 5 minutes documented by monitoring ECG measurements using ECG patches (ePatch) placed on the participant's chest.

All randomized participants who received study treatment and had at least 1 post-dose ECG (by ePatch) by Day 30 post-surgery.

End point type	Secondary
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End point timeframe:

First 30 days following the initial ICU admission date after open-chest cardiac surgery.

End point values	Placebo	AGN-151607 (125 U)	AGN-151607 (250 U)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	104	106	
Units: percentage of participants				
number (not applicable)	44.1	34.6	46.2	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).

Comparison groups	AGN-151607 (125 U) v Placebo
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1603
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	1.1

Statistical analysis title	Statistical Analysis 2
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Statistical analysis description:

P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).

Comparison groups	AGN-151607 (250 U) v Placebo
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Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6706
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.42

Secondary: Percentage of Participants With at Least 1 Continuous AF (Atrial Fibrillation or Atrial Flutter) Episode \geq 6 Minutes During the First 30 Days Post-surgery

End point title	Percentage of Participants With at Least 1 Continuous AF (Atrial Fibrillation or Atrial Flutter) Episode \geq 6 Minutes During the First 30 Days Post-surgery
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End point description:

At least one episode of continuous AF (atrial fibrillation or atrial flutter) sustained \geq 6 minutes documented by monitoring ECG measurements using ECG patches (ePatch) placed on the participant's chest.

All randomized participants who received study treatment and had at least 1 post-dose ECG (by ePatch) by Day 30 post-surgery.

End point type	Secondary
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End point timeframe:

First 30 days following the initial ICU admission date after open-chest cardiac surgery.

End point values	Placebo	AGN-151607 (125 U)	AGN-151607 (250 U)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	104	106	
Units: percentage of participants				
number (not applicable)	43.1	33.7	45.3	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).

Comparison groups	AGN-151607 (125 U) v Placebo
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Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1583
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.1

Statistical analysis title	Statistical Analysis 2
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Statistical analysis description:

P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).

Comparison groups	AGN-151607 (250 U) v Placebo
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6694
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.43

Secondary: Percentage of Participants With at Least 1 Continuous AF (Atrial Fibrillation or Atrial Flutter) Episode ≥ 30 Minutes During the First 30 Days Post-surgery

End point title	Percentage of Participants With at Least 1 Continuous AF (Atrial Fibrillation or Atrial Flutter) Episode ≥ 30 Minutes During the First 30 Days Post-surgery
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End point description:

At least one episode of continuous AF (atrial fibrillation or atrial flutter) sustained ≥ 30 minutes documented by monitoring ECG measurements using ECG patches (ePatch) placed on the participant's chest.

All randomized participants who received study treatment and had at least 1 post-dose ECG (by ePatch) by Day 30 post-surgery.

End point type	Secondary
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End point timeframe:

First 30 days following the initial ICU admission date after open-chest cardiac surgery.

End point values	Placebo	AGN-151607 (125 U)	AGN-151607 (250 U)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	104	106	
Units: percentage of participants				
number (not applicable)	38.2	30.8	39.6	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).	
Comparison groups	AGN-151607 (125 U) v Placebo
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2578
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.18

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).	
Comparison groups	AGN-151607 (250 U) v Placebo
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7526
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	1.05

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.47

Secondary: Percentage of Participants With at Least 1 Continuous AF (Atrial Fibrillation or Atrial Flutter) Episode \geq 1 Hour During the First 30 Days Post-surgery

End point title	Percentage of Participants With at Least 1 Continuous AF (Atrial Fibrillation or Atrial Flutter) Episode \geq 1 Hour During the First 30 Days Post-surgery
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End point description:

At least one episode of continuous AF (atrial fibrillation or atrial flutter) sustained \geq 1 hour documented by monitoring ECG measurements using ECG patches (ePatch) placed on the participant's chest.

All randomized participants who received study treatment and had at least 1 post-dose ECG (by ePatch) by Day 30 post-surgery.

End point type	Secondary
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End point timeframe:

First 30 days following the initial ICU admission date after open-chest cardiac surgery.

End point values	Placebo	AGN-151607 (125 U)	AGN-151607 (250 U)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	104	106	
Units: percentage of participants				
number (not applicable)	37.3	29.8	37.7	

Statistical analyses

Statistical analysis title	Statistical Analysis 2
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Statistical analysis description:

P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).

Comparison groups	AGN-151607 (250 U) v Placebo
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8544
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	1.03

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.45

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).

Comparison groups	AGN-151607 (125 U) v Placebo
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2549
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.18

Secondary: Percentage of Participants With at Least 1 Continuous AF (Atrial Fibrillation or Atrial Flutter) Episode ≥ 4 Hours During the First 30 Days Post-surgery

End point title	Percentage of Participants With at Least 1 Continuous AF (Atrial Fibrillation or Atrial Flutter) Episode ≥ 4 Hours During the First 30 Days Post-surgery
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End point description:

At least one episode of continuous AF (atrial fibrillation or atrial flutter) sustained ≥ 4 hours documented by monitoring ECG measurements using ECG patches (ePatch) placed on the participant's chest.

All randomized participants who received study treatment and had at least 1 post-dose ECG (by ePatch) by Day 30 post-surgery.

End point type	Secondary
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End point timeframe:

First 30 days following the initial ICU admission date after open-chest cardiac surgery.

End point values	Placebo	AGN-151607 (125 U)	AGN-151607 (250 U)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	104	106	
Units: percentage of participants				
number (not applicable)	32.4	24.0	26.4	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).	
Comparison groups	AGN-151607 (125 U) v Placebo
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1718
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	1.14

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).	
Comparison groups	AGN-151607 (250 U) v Placebo
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3801
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	1.27

Secondary: Percentage of Participants With at Least 1 Continuous AF (Atrial Fibrillation or Atrial Flutter) Episode \geq 6 Hours During the First 30 Days Post-surgery

End point title	Percentage of Participants With at Least 1 Continuous AF (Atrial Fibrillation or Atrial Flutter) Episode \geq 6 Hours During the First 30 Days Post-surgery
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End point description:

At least one episode of continuous AF (atrial fibrillation or atrial flutter) sustained \geq 6 hours documented by monitoring ECG measurements using ECG patches (ePatch) placed on the participant's chest.

All randomized participants who received study treatment and had at least 1 post-dose ECG (by ePatch) by Day 30 post-surgery.

End point type	Secondary
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End point timeframe:

First 30 days following the initial ICU admission date after open-chest cardiac surgery.

End point values	Placebo	AGN-151607 (125 U)	AGN-151607 (250 U)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	104	106	
Units: percentage of participants				
number (not applicable)	25.5	22.1	20.8	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).

Comparison groups	AGN-151607 (125 U) v Placebo
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5531
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	1.39

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).	
Comparison groups	AGN-151607 (250 U) v Placebo
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4213
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	1.33

Secondary: Percentage of Participants With at Least 1 Continuous AF (Atrial Fibrillation or Atrial Flutter) Episode ≥ 12 Hours During the First 30 Days Post-surgery

End point title	Percentage of Participants With at Least 1 Continuous AF (Atrial Fibrillation or Atrial Flutter) Episode ≥ 12 Hours During the First 30 Days Post-surgery
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End point description:

At least one episode of continuous AF (atrial fibrillation or atrial flutter) sustained ≥ 12 hours documented by monitoring ECG measurements using ECG patches (ePatch) placed on the participant's chest.

All randomized participants who received study treatment and had at least 1 post-dose ECG (by ePatch) by Day 30 post-surgery.

End point type	Secondary
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End point timeframe:

First 30 days following the initial ICU admission date after open-chest cardiac surgery.

End point values	Placebo	AGN-151607 (125 U)	AGN-151607 (250 U)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	104	106	
Units: percentage of participants				
number (not applicable)	15.7	14.4	17.0	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).

Comparison groups	AGN-151607 (125 U) v Placebo
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.804
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	1.73

Statistical analysis title

Statistical Analysis 2

Statistical analysis description:

P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).

Comparison groups	AGN-151607 (250 U) v Placebo
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7573
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	1.98

Secondary: Percentage of Participants With at Least 1 Continuous AF (Atrial Fibrillation or Atrial Flutter) Episode ≥ 24 Hours During the First 30 Days Post-surgery

End point title	Percentage of Participants With at Least 1 Continuous AF (Atrial Fibrillation or Atrial Flutter) Episode ≥ 24 Hours During the First 30 Days Post-surgery
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End point description:

At least one episode of continuous AF (atrial fibrillation or atrial flutter) sustained ≥ 24 hours documented by monitoring ECG measurements using ECG patches (ePatch) placed on the participant's chest.

All randomized participants who received study treatment and had at least 1 post-dose ECG (by ePatch) by Day 30 post-surgery.

End point type	Secondary
End point timeframe:	
First 30 days following the initial ICU admission date after open-chest cardiac surgery.	

End point values	Placebo	AGN-151607 (125 U)	AGN-151607 (250 U)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	104	106	
Units: percentage of participants				
number (not applicable)	9.8	6.7	12.3	

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).	
Comparison groups	AGN-151607 (250 U) v Placebo
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5257
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	2.7

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).	
Comparison groups	AGN-151607 (125 U) v Placebo
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4065
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	0.69

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.28
upper limit	1.67

Secondary: Percentage of Participants With at Least 1 Continuous Atrial Fibrillation (Excluding Atrial Flutter) Episode ≥ 30 Seconds During the First 30 Days Post-surgery

End point title	Percentage of Participants With at Least 1 Continuous Atrial Fibrillation (Excluding Atrial Flutter) Episode ≥ 30 Seconds During the First 30 Days Post-surgery
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End point description:

At least one episode of continuous atrial fibrillation (excluding atrial flutter) sustained ≥ 30 seconds documented by monitoring ECG measurements using ECG patches (ePatch) placed on the participant's chest.

All randomized participants who received study treatment and had at least 1 post-dose ECG (by ePatch) by Day 30 post-surgery.

End point type	Secondary
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End point timeframe:

First 30 days following the initial ICU admission date after open-chest cardiac surgery.

End point values	Placebo	AGN-151607 (125 U)	AGN-151607 (250 U)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	104	106	
Units: percentage of participants				
number (not applicable)	43.1	33.7	42.5	

Statistical analyses

Statistical analysis title	Statistical Analysis 2
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Statistical analysis description:

P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).

Comparison groups	AGN-151607 (250 U) v Placebo
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9966
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	1

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.35

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).

Comparison groups	AGN-151607 (125 U) v Placebo
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1612
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.11

Secondary: Percentage of Participants With at Least 1 Continuous Atrial Flutter Episode ≥ 30 Seconds During the First 30 Days Post-surgery

End point title	Percentage of Participants With at Least 1 Continuous Atrial Flutter Episode ≥ 30 Seconds During the First 30 Days Post-surgery
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End point description:

At least one episode of continuous atrial flutter sustained ≥ 30 seconds documented by monitoring ECG measurements using ECG patches (ePatch) placed on the participant's chest.

All randomized participants who received study treatment and had at least 1 post-dose ECG (by ePatch) by Day 30 post-surgery.

End point type	Secondary
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End point timeframe:

First 30 days following the initial ICU admission date after open-chest cardiac surgery.

End point values	Placebo	AGN-151607 (125 U)	AGN-151607 (250 U)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	104	106	
Units: percentage of participants				
number (not applicable)	12.7	8.7	15.1	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).	
Comparison groups	AGN-151607 (125 U) v Placebo
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3374
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	1.52

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).	
Comparison groups	AGN-151607 (250 U) v Placebo
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5403
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	2.45

Secondary: Percentage of Participants With at Least 1 Continuous Atrial Tachycardia Episode (Defined as the Duration of the Longest Supraventricular Tachycardia [SVT] Run) \geq 30 Seconds During the First 30 Days Post-surgery

End point title	Percentage of Participants With at Least 1 Continuous Atrial Tachycardia Episode (Defined as the Duration of the Longest Supraventricular Tachycardia [SVT] Run) \geq 30 Seconds During the First 30 Days Post-surgery
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End point description:

At least one episode of continuous atrial tachycardia sustained \geq 30 seconds documented by monitoring ECG measurements using ECG patches (ePatch) placed on the participant's chest.

All randomized participants who received study treatment and had at least 1 post-dose ECG (by ePatch) by Day 30 post-surgery.

End point type	Secondary
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End point timeframe:

First 30 days following the initial ICU admission date after open-chest cardiac surgery.

End point values	Placebo	AGN-151607 (125 U)	AGN-151607 (250 U)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	104	106	
Units: percentage of participants				
number (not applicable)	2.9	11.5	7.5	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).

Comparison groups	AGN-151607 (125 U) v Placebo
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0163
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	3.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.16
upper limit	13.42

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).	
Comparison groups	AGN-151607 (250 U) v Placebo
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1101
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	9.64

Secondary: Percentage of Participants With at Least 1 Continuous Episode of Either Atrial Fibrillation or Atrial Flutter or Atrial Tachycardia ≥ 30 Seconds During the First 30 Days Post-surgery

End point title	Percentage of Participants With at Least 1 Continuous Episode of Either Atrial Fibrillation or Atrial Flutter or Atrial Tachycardia ≥ 30 Seconds During the First 30 Days Post-surgery
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End point description:

At least one episode of continuous atrial fibrillation or atrial flutter or atrial tachycardia sustained ≥ 30 seconds documented by monitoring ECG measurements using ECG patches (ePatch) placed on the participant's chest.

All randomized participants who received study treatment and had at least 1 post-dose ECG (by ePatch) by Day 30 post-surgery.

End point type	Secondary
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End point timeframe:

First 30 days following the initial ICU admission date after open-chest cardiac surgery.

End point values	Placebo	AGN-151607 (125 U)	AGN-151607 (250 U)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	104	106	
Units: percentage of participants				
number (not applicable)	48.0	41.3	51.9	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).	
Comparison groups	AGN-151607 (125 U) v Placebo
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3339
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	1.16

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
P-values and Risk Ratios (and their corresponding 95% CI) for each pairwise comparison of AGN-151607 versus Placebo are obtained from Cochran-Mantel-Haenszel (CMH) test controlling for type of surgery (presence or absence of valve surgery) and age group (< 65 or ≥ 65 years).	
Comparison groups	AGN-151607 (250 U) v Placebo
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4614
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk ratio (RR)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.42

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The length of this study was up to 367 days post single dose study treatment, plus up to 28 days before the first study day (randomization, Day 1).

Adverse event reporting additional description:

Of the 323 subjects enrolled and included in the All-cause mortality data table, 4 did not receive treatment and, therefore, did not go beyond the 28-Day screening period. The median time that the 319 subjects who received a single treatment of Placebo, AGN-151607 125 Units, or AGN-151607250 Units was 371.0, 372.0 and 371.0 days, respectively.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	PLACEBO
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Reporting group description: -

Reporting group title	AGN-151607_250_U
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Reporting group description: -

Reporting group title	AGN-151607_125_U
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Reporting group description: -

Serious adverse events	PLACEBO	AGN-151607_250_U	AGN-151607_125_U
Total subjects affected by serious adverse events			
subjects affected / exposed	36 / 105 (34.29%)	28 / 109 (25.69%)	38 / 105 (36.19%)
number of deaths (all causes)	1	2	0
number of deaths resulting from adverse events	1	2	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
LUNG NEOPLASM			
subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NON-SMALL CELL LUNG CANCER			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG ADENOCARCINOMA			

subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL CANCER			
subjects affected / exposed	0 / 105 (0.00%)	1 / 109 (0.92%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
SHOCK HAEMORRHAGIC			
subjects affected / exposed	0 / 105 (0.00%)	1 / 109 (0.92%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
AORTIC PERFORATION			
subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEEP VEIN THROMBOSIS			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THROMBOSIS			
subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMORRHAGE			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTENSION			
subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERMITTENT CLAUDICATION			

subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ORTHOSTATIC HYPOTENSION			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMATOMA			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	2 / 105 (1.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYREXIA			
subjects affected / exposed	1 / 105 (0.95%)	1 / 109 (0.92%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
PNEUMOTHORAX			
subjects affected / exposed	0 / 105 (0.00%)	1 / 109 (0.92%)	3 / 105 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY EMBOLISM			
subjects affected / exposed	5 / 105 (4.76%)	2 / 109 (1.83%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURAL EFFUSION			
subjects affected / exposed	3 / 105 (2.86%)	1 / 109 (0.92%)	2 / 105 (1.90%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

HAEMOTHORAX			
subjects affected / exposed	0 / 105 (0.00%)	1 / 109 (0.92%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSпноEA EXERTIONAL			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSпноEA			
subjects affected / exposed	1 / 105 (0.95%)	1 / 109 (0.92%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIAPHRAGMATIC PARALYSIS			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASPIRATION			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY OEDEMA			
subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY FAILURE			

subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
MENTAL STATUS CHANGES			
subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMOGLOBIN DECREASED			
subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERNATIONAL NORMALISED RATIO INCREASED			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ELECTROENCEPHALOGRAM ABNORMAL			

subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
CORONARY SINUS INJURY			
subjects affected / exposed	0 / 105 (0.00%)	1 / 109 (0.92%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FALL			
subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPROCEDURAL MYOCARDIAL INFARCTION			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POST PROCEDURAL HAEMORRHAGE			
subjects affected / exposed	2 / 105 (1.90%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POSTOPERATIVE ILEUS			
subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PROCEDURAL HAEMORRHAGE			
subjects affected / exposed	0 / 105 (0.00%)	1 / 109 (0.92%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRANSFUSION-RELATED ACUTE LUNG INJURY			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

SUBDURAL HAEMATOMA			
subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VASCULAR GRAFT OCCLUSION			
subjects affected / exposed	0 / 105 (0.00%)	1 / 109 (0.92%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VASCULAR PROCEDURE COMPLICATION			
subjects affected / exposed	0 / 105 (0.00%)	1 / 109 (0.92%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
AORTIC VALVE INCOMPETENCE			
subjects affected / exposed	0 / 105 (0.00%)	1 / 109 (0.92%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIAL FIBRILLATION			
subjects affected / exposed	6 / 105 (5.71%)	4 / 109 (3.67%)	6 / 105 (5.71%)
occurrences causally related to treatment / all	0 / 7	0 / 6	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIAL FLUTTER			
subjects affected / exposed	5 / 105 (4.76%)	5 / 109 (4.59%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 5	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIOVENTRICULAR BLOCK			
subjects affected / exposed	0 / 105 (0.00%)	1 / 109 (0.92%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIOVENTRICULAR BLOCK COMPLETE			
subjects affected / exposed	1 / 105 (0.95%)	2 / 109 (1.83%)	2 / 105 (1.90%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

BRADYCARDIA			
subjects affected / exposed	0 / 105 (0.00%)	2 / 109 (1.83%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC ARREST			
subjects affected / exposed	0 / 105 (0.00%)	1 / 109 (0.92%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
CARDIAC FAILURE			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC FAILURE ACUTE			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIOGENIC SHOCK			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE LEFT VENTRICULAR FAILURE			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERICARDIAL EFFUSION			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NODAL RHYTHM			

subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYOCARDIAL ISCHAEMIA			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORONARY ARTERY PERFORATION			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORONARY ARTERY DISEASE			
subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERICARDITIS			
subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
FACIAL PARALYSIS			
subjects affected / exposed	0 / 105 (0.00%)	1 / 109 (0.92%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOSS OF CONSCIOUSNESS			
subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRANSIENT ISCHAEMIC ATTACK			

subjects affected / exposed	1 / 105 (0.95%)	1 / 109 (0.92%)	2 / 105 (1.90%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYNCOPE			
subjects affected / exposed	1 / 105 (0.95%)	1 / 109 (0.92%)	3 / 105 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYASTHENIA GRAVIS			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENCEPHALOPATHY			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIZZINESS			
subjects affected / exposed	0 / 105 (0.00%)	1 / 109 (0.92%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	3 / 105 (2.86%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CEREBRAL ISCHAEMIA			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BELL'S PALSY			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
AMYOTROPHIC LATERAL SCLEROSIS			

subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
BLOOD LOSS ANAEMIA			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAEMIA			
subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	2 / 105 (1.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COAGULOPATHY			
subjects affected / exposed	0 / 105 (0.00%)	1 / 109 (0.92%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THROMBOCYTOSIS			
subjects affected / exposed	0 / 105 (0.00%)	1 / 109 (0.92%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
DIPLOPIA			
subjects affected / exposed	0 / 105 (0.00%)	2 / 109 (1.83%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
MELAENA			
subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ILEUS			
subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

GASTROINTESTINAL HAEMORRHAGE	subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
	occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
	deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPHAGIA	subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
	occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
	deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA	subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
	occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
	deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
AORTO-OESOPHAGEAL FISTULA	subjects affected / exposed	0 / 105 (0.00%)	1 / 109 (0.92%)	0 / 105 (0.00%)
	occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
	deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hepatobiliary disorders				
CHOLECYSTITIS ACUTE	subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
	occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
	deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders				
ACUTE KIDNEY INJURY	subjects affected / exposed	2 / 105 (1.90%)	1 / 109 (0.92%)	0 / 105 (0.00%)
	occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
	deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMATURIA	subjects affected / exposed	0 / 105 (0.00%)	1 / 109 (0.92%)	0 / 105 (0.00%)
	occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
	deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEPHROLITHIASIS	subjects affected / exposed	0 / 105 (0.00%)	1 / 109 (0.92%)	1 / 105 (0.95%)
	occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
	deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

URINARY RETENTION			
subjects affected / exposed	0 / 105 (0.00%)	1 / 109 (0.92%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
MUSCULAR WEAKNESS			
subjects affected / exposed	0 / 105 (0.00%)	1 / 109 (0.92%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ROTATOR CUFF SYNDROME			
subjects affected / exposed	0 / 105 (0.00%)	1 / 109 (0.92%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
APPENDICITIS			
subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENDOCARDITIS			
subjects affected / exposed	0 / 105 (0.00%)	1 / 109 (0.92%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIVERTICULITIS			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MEDIASTINITIS			
subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	2 / 105 (1.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 105 (0.00%)	1 / 109 (0.92%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

COLONIC ABSCESS			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CELLULITIS			
subjects affected / exposed	2 / 105 (1.90%)	1 / 109 (0.92%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHITIS			
subjects affected / exposed	0 / 105 (0.00%)	1 / 109 (0.92%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACTERAEMIA			
subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 PNEUMONIA			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
OSTEOMYELITIS			
subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	1 / 105 (0.95%)	1 / 109 (0.92%)	2 / 105 (1.90%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPSIS			
subjects affected / exposed	1 / 105 (0.95%)	0 / 109 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			

subjects affected / exposed	0 / 105 (0.00%)	1 / 109 (0.92%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND INFECTION			
subjects affected / exposed	0 / 105 (0.00%)	0 / 109 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
LACTIC ACIDOSIS			
subjects affected / exposed	1 / 105 (0.95%)	1 / 109 (0.92%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	PLACEBO	AGN-151607_250_U	AGN-151607_125_U
Total subjects affected by non-serious adverse events			
subjects affected / exposed	86 / 105 (81.90%)	94 / 109 (86.24%)	84 / 105 (80.00%)
Vascular disorders			
HYPOTENSION			
subjects affected / exposed	15 / 105 (14.29%)	17 / 109 (15.60%)	10 / 105 (9.52%)
occurrences (all)	18	20	10
HYPERTENSION			
subjects affected / exposed	8 / 105 (7.62%)	6 / 109 (5.50%)	7 / 105 (6.67%)
occurrences (all)	9	6	7
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	2 / 105 (1.90%)	5 / 109 (4.59%)	8 / 105 (7.62%)
occurrences (all)	2	6	8
OEDEMA PERIPHERAL			
subjects affected / exposed	13 / 105 (12.38%)	10 / 109 (9.17%)	10 / 105 (9.52%)
occurrences (all)	15	10	11
FATIGUE			
subjects affected / exposed	7 / 105 (6.67%)	5 / 109 (4.59%)	3 / 105 (2.86%)
occurrences (all)	8	5	3

Respiratory, thoracic and mediastinal disorders			
PNEUMOTHORAX			
subjects affected / exposed	1 / 105 (0.95%)	6 / 109 (5.50%)	7 / 105 (6.67%)
occurrences (all)	1	6	7
PLEURAL EFFUSION			
subjects affected / exposed	14 / 105 (13.33%)	22 / 109 (20.18%)	10 / 105 (9.52%)
occurrences (all)	15	24	11
DYSPNOEA			
subjects affected / exposed	13 / 105 (12.38%)	13 / 109 (11.93%)	3 / 105 (2.86%)
occurrences (all)	19	13	4
COUGH			
subjects affected / exposed	6 / 105 (5.71%)	7 / 109 (6.42%)	3 / 105 (2.86%)
occurrences (all)	7	7	3
ATELECTASIS			
subjects affected / exposed	12 / 105 (11.43%)	18 / 109 (16.51%)	11 / 105 (10.48%)
occurrences (all)	12	20	11
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	16 / 105 (15.24%)	12 / 109 (11.01%)	17 / 105 (16.19%)
occurrences (all)	16	12	17
ANXIETY			
subjects affected / exposed	6 / 105 (5.71%)	5 / 109 (4.59%)	3 / 105 (2.86%)
occurrences (all)	6	5	4
DELIRIUM			
subjects affected / exposed	2 / 105 (1.90%)	6 / 109 (5.50%)	2 / 105 (1.90%)
occurrences (all)	2	6	2
Injury, poisoning and procedural complications			
VASOPLEGIA SYNDROME			
subjects affected / exposed	3 / 105 (2.86%)	13 / 109 (11.93%)	5 / 105 (4.76%)
occurrences (all)	3	13	5
PROCEDURAL PAIN			
subjects affected / exposed	20 / 105 (19.05%)	21 / 109 (19.27%)	20 / 105 (19.05%)
occurrences (all)	20	21	21
Cardiac disorders			
SINUS TACHYCARDIA			

subjects affected / exposed occurrences (all)	7 / 105 (6.67%) 8	2 / 109 (1.83%) 2	1 / 105 (0.95%) 1
PALPITATIONS			
subjects affected / exposed occurrences (all)	7 / 105 (6.67%) 10	6 / 109 (5.50%) 6	4 / 105 (3.81%) 6
BRADYCARDIA			
subjects affected / exposed occurrences (all)	4 / 105 (3.81%) 4	4 / 109 (3.67%) 4	7 / 105 (6.67%) 8
ATRIAL FLUTTER			
subjects affected / exposed occurrences (all)	6 / 105 (5.71%) 6	7 / 109 (6.42%) 7	5 / 105 (4.76%) 6
ATRIAL FIBRILLATION			
subjects affected / exposed occurrences (all)	32 / 105 (30.48%) 38	35 / 109 (32.11%) 40	31 / 105 (29.52%) 37
TACHYCARDIA			
subjects affected / exposed occurrences (all)	4 / 105 (3.81%) 4	12 / 109 (11.01%) 12	4 / 105 (3.81%) 6
Nervous system disorders			
DIZZINESS			
subjects affected / exposed occurrences (all)	8 / 105 (7.62%) 10	5 / 109 (4.59%) 5	4 / 105 (3.81%) 4
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed occurrences (all)	27 / 105 (25.71%) 28	30 / 109 (27.52%) 30	19 / 105 (18.10%) 20
Gastrointestinal disorders			
VOMITING			
subjects affected / exposed occurrences (all)	4 / 105 (3.81%) 4	7 / 109 (6.42%) 7	2 / 105 (1.90%) 2
NAUSEA			
subjects affected / exposed occurrences (all)	25 / 105 (23.81%) 25	29 / 109 (26.61%) 30	25 / 105 (23.81%) 27
CONSTIPATION			
subjects affected / exposed occurrences (all)	10 / 105 (9.52%) 10	6 / 109 (5.50%) 6	7 / 105 (6.67%) 9
Skin and subcutaneous tissue disorders			

DERMATITIS CONTACT subjects affected / exposed occurrences (all)	5 / 105 (4.76%) 5	6 / 109 (5.50%) 6	2 / 105 (1.90%) 2
Musculoskeletal and connective tissue disorders MUSCULOSKELETAL CHEST PAIN subjects affected / exposed occurrences (all)	12 / 105 (11.43%) 12	9 / 109 (8.26%) 9	11 / 105 (10.48%) 12
Infections and infestations URINARY TRACT INFECTION subjects affected / exposed occurrences (all) COVID-19 subjects affected / exposed occurrences (all)	4 / 105 (3.81%) 4 5 / 105 (4.76%) 5	6 / 109 (5.50%) 6 6 / 109 (5.50%) 6	6 / 105 (5.71%) 7 10 / 105 (9.52%) 12
Metabolism and nutrition disorders HYPOPHOSPHATAEMIA subjects affected / exposed occurrences (all) HYPOKALAEMIA subjects affected / exposed occurrences (all) HYPERVOLAEMIA subjects affected / exposed occurrences (all) HYPERGLYCAEMIA subjects affected / exposed occurrences (all)	5 / 105 (4.76%) 5 3 / 105 (2.86%) 3 18 / 105 (17.14%) 19 14 / 105 (13.33%) 16	7 / 109 (6.42%) 7 9 / 109 (8.26%) 9 23 / 109 (21.10%) 23 17 / 109 (15.60%) 17	6 / 105 (5.71%) 6 3 / 105 (2.86%) 3 24 / 105 (22.86%) 24 17 / 105 (16.19%) 19

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 September 2020	The purpose of this protocol amendment was to clarify specific points within the protocol based on clinical experience to date. These changes did not impact the safety assessment of botulinum toxin type A or alter the risk-benefit ratio for study participants. Administrative edits were also made, but not specifically noted (eg, corrected spelling, punctuation, grammar, abbreviations, and style errors) including global edits required for consistency (eg, “study drug”, “participants”, abbreviation use).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported