Clinical trial results:
An Open-label, Single-dose, Pharmacokinetic Study to Evaluate IV Eptinezumab in Children and Adolescents with Migraine, Followed by an Optional, Multiple-dose, Open-label Extension Period

Summary

EudraCT number	2022-004102-29
Trial protocol	Outside EU/EEA
Global end of trial date	

Results information

Result version number	v1
This version publication date	15 April 2023
First version publication date	15 April 2023

Trial information

Trial identification

Sponsor protocol code	18922A

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04537429
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	H. Lundbeck A/S
Sponsor organisation address	Ottiliavej 9, Valby, Denmark, 2500
Public contact	LundbeckClinicalTrials@lundbeck.com, H. Lundbeck A/S, +45 36301311, LundbeckClinicalTrials@lundbeck.com
Scientific contact	LundbeckClinicalTrials@lundbeck.com, H. Lundbeck A/S, +45 36301311, LundbeckClinicalTrials@lundbeck.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002243-PIP01-17
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?	Yes

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	20 October 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 October 2022
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial is to characterize the pharmacokinetics (PK) profile of eptinezumab after a single intravenous (IV) administration in pediatric participants 6 to 17 years of age.

Protection of trial subjects:

This study is being conducted in compliance with Good Clinical Practice and in accordance with the ethical principles described in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 August 2020
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 States: 28
Worldwide total number of subjects	28
EEA total number of subjects	0

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)	12
Adolescents (12-17 years)	16
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study consists of a single-dose, 20-week Main Study Period (Part A) and an optional 44-week multiple-dose Extension Period (Part B). The data collected during the completed Main Study Period (Part A) are presented. The data from the ongoing Extension Period (Part B) will be presented when the study has been completed.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Eptinezumab (Age Group 6 to 11 Years)

Arm description:

Participants received a single dose of eptinezumab on Day 1 based on the highest target adult exposure of eptinezumab, adjusted for the participant's body weight.

Arm type	Experimental
Investigational medicinal product name	Eptinezumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Eptinezumab will be administered per schedule specified in the arm description.

Arm title	Eptinezumab (Age Group 12 to 17 Years)

Arm description:

Participants received a single dose of eptinezumab on Day 1 based on the highest target adult exposure of eptinezumab, adjusted for the participant's body weight.

Arm type	Experimental
Investigational medicinal product name	Eptinezumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Eptinezumab will be administered per schedule specified in the arm description.

Number of subjects in period 1	Eptinezumab (Age Group 6 to 11 Years)	Eptinezumab (Age Group 12 to 17 Years)
Started	12	16
Received at least 1 dose of study drug	12	16
Completed	11	14
Not completed	1	2
Consent withdrawn by subject	1	-
Other than specified	-	1
Lost to follow-up	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Eptinezumab (Age Group 6 to 11 Years)
Reporting group description:	
Participants received a single dose of eptinezumab on Day 1 based on the highest target adult exposure of eptinezumab, adjusted for the participant's body weight.	
Reporting group title	Eptinezumab (Age Group 12 to 17 Years)
Reporting group description:	
Participants received a single dose of eptinezumab on Day 1 based on the highest target adult exposure of eptinezumab, adjusted for the participant's body weight.	

Reporting group values	Eptinezumab (Age Group 6 to 11 Years)	Eptinezumab (Age Group 12 to 17 Years)	Total
Number of subjects	12	16	28
Age Categorical Units: Subjects			
Children (2-11 years)	12	0	12
Adolescents (12-17 years)	0	16	16
Age Continuous Units: years			
arithmetic mean	9.3	15.1	
standard deviation	± 1.97	± 1.41	-
Gender Categorical Units: Subjects			
Female	10	10	20
Male	2	6	8
Ethnicity Units: Subjects			
Hispanic or Latino	1	5	6
Not Hispanic or Latino	11	11	22
Race Units: Subjects			
Asian	1	0	1
Black or African American	1	1	2
White or Caucasian	9	15	24
Other	1	0	1

End points

End points reporting groups

Reporting group title	Eptinezumab (Age Group 6 to 11 Years)
Reporting group description:	
Participants received a single dose of eptinezumab on Day 1 based on the highest target adult exposure of eptinezumab, adjusted for the participant's body weight.	
Reporting group title	Eptinezumab (Age Group 12 to 17 Years)
Reporting group description:	
Participants received a single dose of eptinezumab on Day 1 based on the highest target adult exposure of eptinezumab, adjusted for the participant's body weight.	

Primary: Part A: Area Under the Concentration Versus Time Curve From Time Zero to Infinity (AUC0-inf) of Eptinezumab

End point title	Part A: Area Under the Concentration Versus Time Curve From Time Zero to Infinity (AUC0-inf) of Eptinezumab[1]
End point description:	
PK Part A set (PKS_A) included all treated participants in Part A with at least 1 post-infusion PK sample in Part A. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint. n = participants evaluable for specified category. '99999' signifies 'data not available since no participants were evaluable in that category'. '9999' signifies 'due to single participant, geometric coefficient of variation data could not be calculated'.	
End point type	Primary
End point timeframe:	
Day 1 (the day of infusion) through Week 20	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The statistical analysis was not planned for this endpoint.

End point values	Eptinezumab (Age Group 6 to 11 Years)	Eptinezumab (Age Group 12 to 17 Years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	15		
Units: hours*micrograms (µg)/milliliter (mL)				
geometric mean (geometric coefficient of variation)				
Weight Group >20 kg - <=40 kg (n=10,0)	87780 (± 33.1)	99999 (± 99999)		
Weight Group >40 kg (n=1,15)	141700 (± 9999)	91520 (± 15.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Maximum Observed Plasma Concentration (Cmax) of Eptinezumab

End point title	Part A: Maximum Observed Plasma Concentration (Cmax) of Eptinezumab[2]

End point description:

PKS_A included all treated participants in Part A with at least 1 post-infusion PK sample in Part A. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint. n = participants evaluable for specified category. '99999' signifies 'data not available since no participants were evaluable in that category'. '9999' signifies 'due to single participant, geometric coefficient of variation data could not be calculated'.

End point type	Primary

End point timeframe:

Day 1 (the day of infusion) through Week 20

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The statistical analysis was not planned for this endpoint.

End point values	Eptinezumab (Age Group 6 to 11 Years)	Eptinezumab (Age Group 12 to 17 Years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	16		
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Weight Group >20 kg - <=40 kg (n=11,0)	126.2 (± 31.9)	99999 (± 99999)		
Weight Group >40 kg (n=1,16)	215.7 (± 9999)	129.7 (± 32.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Area Under the Concentration Versus Time Curve From Time Zero to the Time of Last Quantifiable Concentration (AUC0-t last) of Eptinezumab

End point title	Part A: Area Under the Concentration Versus Time Curve From Time Zero to the Time of Last Quantifiable Concentration (AUC0-t last) of Eptinezumab

End point description:

PKS_A included all treated participants in Part A with at least 1 post-infusion PK sample in Part A. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint. n = participants evaluable for specified category. '99999' signifies 'data not available since no participants were evaluable in that category'. '9999' signifies 'due to single participant, geometric coefficient of variation data could not be calculated'.

End point type	Secondary

End point timeframe:

Day 1 (the day of infusion) through Week 20

End point values	Eptinezumab (Age Group 6 to 11 Years)	Eptinezumab (Age Group 12 to 17 Years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	16		
Units: hours*µg/mL				
geometric mean (geometric coefficient of variation)				
Weight Group >20 kg - <=40 kg (n=11,0)	79260 (± 40.6)	99999 (± 99999)		
Weight Group >40 kg (n=1,16)	138000 (± 9999)	86500 (± 15.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Concentration for Eptinezumab Determined From the Data Without Interpolation at Week 12 (C12wk)

End point title	Part A: Concentration for Eptinezumab Determined From the Data Without Interpolation at Week 12 (C12wk)

End point description:

PKS_A included all treated participants in Part A with at least 1 post-infusion PK sample in Part A. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint. n = participants evaluable for specified category. '99999' signifies 'data not available since no participants were evaluable in that category'. '9999' signifies 'due to single participant, geometric coefficient of variation data could not be calculated'.

End point type	Secondary

End point timeframe:

Week 12

End point values	Eptinezumab (Age Group 6 to 11 Years)	Eptinezumab (Age Group 12 to 17 Years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	15		
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Weight Group >20 kg - <=40 kg (n=10,0)	6.440 (± 117)	99999 (± 99999)		
Weight Group >40 kg (n=1,15)	13.38 (± 9999)	9.502 (± 28.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Time to Reach Cmax (tmax) of Eptinezumab

End point title	Part A: Time to Reach Cmax (tmax) of Eptinezumab

End point description:

PKS_A included all treated participants in Part A with at least 1 post-infusion PK sample in Part A. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint. n = participants evaluable for specified category. '99999' signifies 'data not available since no participants were evaluable in that category'.

End point type	Secondary

End point timeframe:

Day 1 (the day of infusion) through Week 20

End point values	Eptinezumab (Age Group 6 to 11 Years)	Eptinezumab (Age Group 12 to 17 Years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	16		
Units: hours				
median (inter-quartile range (Q1-Q3))				
Weight Group >20 kg - <=40 kg (n=11,0)	0.6830 (0.5830 to 2.500)	99999 (99999 to 99999)		
Weight Group >40 kg (n=1,16)	2.617 (2.617 to 2.617)	1.708 (0.6165 to 2.675)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Terminal Elimination Half-life (t1/2) of Eptinezumab

End point title	Part A: Terminal Elimination Half-life (t1/2) of Eptinezumab

End point description:

PKS_A included all treated participants in Part A with at least 1 post-infusion PK sample in Part A. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint. n = participants evaluable for specified category. '99999' signifies 'data not available since no participants were evaluable in that category'.

End point type	Secondary

End point timeframe:

Day 1 (the day of infusion) through Week 20

End point values	Eptinezumab (Age Group 6 to 11 Years)	Eptinezumab (Age Group 12 to 17 Years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	15		
Units: hours				
median (inter-quartile range (Q1-Q3))				
Weight Group >20 kg - <=40 kg (n=10,0)	659.5 (584.5 to 729.9)	99999 (99999 to 99999)		

Weight Group >40 kg (n=1,15)	697.3 (697.3 to 697.3)	702.4 (609.2 to 800.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Plasma Clearance (CL) of Eptinezumab

End point title	Part A: Plasma Clearance (CL) of Eptinezumab

End point description:

PKS_A included all treated participants in Part A with at least 1 post-infusion PK sample in Part A. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint. n = participants evaluable for specified category. '99999' signifies 'data not available since no participants were evaluable in that category'. '9999' signifies 'due to single participant, geometric coefficient of variation data could not be calculated'.

End point type	Secondary

End point timeframe:

Day 1 (the day of infusion) through Week 20

End point values	Eptinezumab (Age Group 6 to 11 Years)	Eptinezumab (Age Group 12 to 17 Years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	15		
Units: liters/hour				
geometric mean (geometric coefficient of variation)				
Weight Group >20 kg - <=40 kg (n=10,0)	0.001709 (± 33.1)	99999 (± 99999)		
Weight Group >40 kg (n=1,15)	0.002118 (± 9999)	0.003278 (± 15.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Volume of Distribution (Vz) of Eptinezumab

End point title	Part A: Volume of Distribution (Vz) of Eptinezumab

End point description:

PKS_A included all treated participants in Part A with at least 1 post-infusion PK sample in Part A. Here, 'Overall number of participants analyzed' = participants evaluable for this endpoint. n = participants evaluable for specified category. '99999' signifies 'data not available since no participants were evaluable in that category'. '9999' signifies 'due to single participant, geometric coefficient of variation data could not be calculated'.

End point type	Secondary

End point timeframe:

Day 1 (the day of infusion) through Week 20

End point values	Eptinezumab (Age Group 6 to 11 Years)	Eptinezumab (Age Group 12 to 17 Years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	15		
Units: liters				
geometric mean (geometric coefficient of variation)				
Weight Group >20 kg - <=40 kg (n=10,0)	1.591 (± 33.7)	99999 (± 99999)		
Weight Group >40 kg (n=1,15)	2.130 (± 9999)	3.324 (± 25.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Number of Participants With Binding Anti-Drug Antibodies (ADAs)

End point title	Part A: Number of Participants With Binding Anti-Drug Antibodies (ADAs)

End point description:

Number of participants with positive ADAs are reported. All-patients-treated in Part A set (APTS_A) included all participants treated with eptinezumab in Part A. Here, 'overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 20

End point values	Eptinezumab (Age Group 6 to 11 Years)	Eptinezumab (Age Group 12 to 17 Years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	14		
Units: participants	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Number of Participants With Neutralizing Binding ADA (NAb)

End point title	Part A: Number of Participants With Neutralizing Binding ADA

	(NAb)

End point description:

Number of participants with non-reactive NAbs are reported. APTS_A included all participants treated with eptinezumab in Part A. Here, 'overall number of participants analyzed' = participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 20

End point values	Eptinezumab (Age Group 6 to 11 Years)	Eptinezumab (Age Group 12 to 17 Years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	14		
Units: participants	0	2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to Week 20	
Adverse event reporting additional description:	
APTS_A included all participants treated with eptinezumab in Part A.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Eptinezumab (Age Group 12 to 17 Years)
Reporting group description:	
Participants received a single dose of eptinezumab on Day 1 based on the highest target adult exposure of eptinezumab, adjusted for the participant's body weight.	
Reporting group title	Eptinezumab (Age Group 6 to 11 Years)
Reporting group description:	
Participants received a single dose of eptinezumab on Day 1 based on the highest target adult exposure of eptinezumab, adjusted for the participant's body weight.	

Serious adverse events	Eptinezumab (Age Group 12 to 17 Years)	Eptinezumab (Age Group 6 to 11 Years)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	0 / 12 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Eptinezumab (Age Group 12 to 17 Years)	Eptinezumab (Age Group 6 to 11 Years)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 16 (56.25%)	7 / 12 (58.33%)	
Investigations			
Blood calcium increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Weight increased			

alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Accidental overdose			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Vascular disorders			
Orthostatic hypotension			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 16 (18.75%)	0 / 12 (0.00%)	
occurrences (all)	4	0	
Nervous system disorders			
Migraine			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Dizziness			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Iron deficiency anaemia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Eye disorders			
Photopsia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 16 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Epistaxis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Cough			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Pruritus			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Depression			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Anxiety			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Adjustment disorder with depressed mood			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Sleep terror			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Renal and urinary disorders			

Proteinuria			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Infections and infestations			
COVID-19			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Gastroenteritis viral			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Influenza			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Pharyngitis streptococcal			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Pyuria			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Urinary tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Vitamin D deficiency			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Hypertriglyceridaemia			

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Vitamin B12 deficiency			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 12 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 November 2020	- Added the eDiary and in consequence, added 2 exploratory endpoints related to the eDiary and updated the screening period to 4 weeks. - Inclusion criterion: upper percentile limit of Centers for Disease Control and Prevention growth charts changed from 95th to 97th percentile. - Inclusion criterion: specification of adequate method of contraception. - Added description of potential mitigations due to COVID-19 pandemic. - Added that re-screening of participants for other reasons than safety concerns may be granted. - Updated that use of acute medication was allowed if dose had been stable for ≥2 weeks; minimum required period prior to screening visits reduced from ≥12 to ≥2 weeks.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported