



Clinical trial results:

A Phase I/II Dose-escalation and Expansion Cohort Trial of Intracerebroventricular Radioimmunotherapy Using ¹⁷⁷Lu-DTPA-omburtamab in Pediatric and Adolescent Patients with Recurrent or Refractory Medulloblastoma

Summary

EudraCT number	2020-000670-22
Trial protocol	GB DK
Global end of trial date	11 August 2022

Results information

Result version number	v1 (current)
This version publication date	28 October 2023
First version publication date	28 October 2023

Trial information

Trial identification

Sponsor protocol code	301
-----------------------	-----

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04167618
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Y-mAbs Therapeutics Inc.
Sponsor organisation address	230 Park Avenue, Suite 3350, New York, United States, NY 10169
Public contact	GRS associate, 'Y-mAbs Therapeutics Inc, +45 70261414, clinicaltrials@ymabs.com
Scientific contact	GRS associate, 'Y-mAbs Therapeutics Inc, +45 70261414, clinicaltrials@ymabs.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	16 December 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 August 2022
Global end of trial reached?	Yes
Global end of trial date	11 August 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of Part 1 (dose-escalation phase) of this trial is to explore the tolerability of up to 2 cycles of intracerebroventricular ¹⁷⁷Lu-DTPA-omburtamab treatment in pediatric and adolescent patients with recurrent or refractory medulloblastoma. The MTD and/or the recommended Phase 2 dose for Part 2 will be determined.

The primary objective of Part 2 (cohort-expansion phase) of this trial is to establish a safety profile of repeated dosing of ¹⁷⁷Lu-DTPA-omburtamab in pediatric and adolescent patients with recurrent or refractory medulloblastoma.

Protection of trial subjects:

This trial will be conducted in accordance with the protocol and with the following:

- Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines
- Ethical considerations for clinical trials on medicinal products conducted with minors
- Applicable International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines
- Applicable laws and regulations.

The protocol, protocol amendments, patient information, ICF, investigator's brochure, and other relevant documents (e.g., advertisements) must be submitted to an Institutional Review Board (IRB)/Ethics Committee (EC) by the investigator and reviewed and approved by the IRB/EC before the trial is initiated.

- Any amendments to the protocol will require regulatory and IRB/EC approval before implementation of changes made to the trial design, except for changes necessary to eliminate an immediate hazard to trial patients.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 September 2021
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	Denmark: 1
Country: Number of subjects enrolled	United States: 1
Worldwide total number of subjects	2
EEA total number of subjects	1

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)	1
Adolescents (12-17 years)	1
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:

All screening evaluations must be completed and reviewed to confirm that potential patients meet all eligibility criteria. The investigator will maintain a screening log to record details of all patients screened and to confirm eligibility or record reasons for screening failure, as applicable.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	10 mCi 177Lu-DTPA-omburtamab

Arm description:

Intracerebroventricular administration of 10 mCi 177Lu-DTPA-omburtamab for up to two cycles (Part 1).

Arm type	Experimental
Investigational medicinal product name	177Lu-DTPA-omburtamab (Biological, radiolabeled DTPA-omburtamab)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intracerebroventricular use

Dosage and administration details:

Intracerebroventricular administration of 10 mCi 177Lu-DTPA-omburtamab for up to two cycles (Part 1).

Arm title	25 mCi 177Lu-DTPA-omburtamab
------------------	------------------------------

Arm description:

Intracerebroventricular administration of 25 mCi 177Lu-DTPA-omburtamab for up to two cycles (Part 1).

Arm type	Experimental
Investigational medicinal product name	177Lu-DTPA-omburtamab (Biological, radiolabeled DTPA-omburtamab)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intracerebroventricular use

Dosage and administration details:

Intracerebroventricular administration of 25 mCi 177Lu-DTPA-omburtamab for up to two cycles (Part 1).

Number of subjects in period 1	10 mCi 177Lu-DTPA-omburtamab	25 mCi 177Lu-DTPA-omburtamab
Started	1	1
Completed	0	0
Not completed	1	1
early termination of trial	1	1

Baseline characteristics

Reporting groups

Reporting group title	10 mCi 177Lu-DTPA-omburtamab
Reporting group description: Intracerebroventricular administration of 10 mCi 177Lu-DTPA-omburtamab for up to two cycles (Part 1).	

Reporting group title	25 mCi 177Lu-DTPA-omburtamab
Reporting group description: Intracerebroventricular administration of 25 mCi 177Lu-DTPA-omburtamab for up to two cycles (Part 1).	

Reporting group values	10 mCi 177Lu-DTPA-omburtamab	25 mCi 177Lu-DTPA-omburtamab	Total
Number of subjects	1	1	2
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	1	0	1
Adolescents (12-17 years)	0	1	1
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	15	8	
full range (min-max)	15 to 15	8 to 8	-
Gender categorical			
Units: Subjects			
Female	0	0	0
Male	1	1	2
Race			
Units: Subjects			
White	1	1	2

End points

End points reporting groups

Reporting group title	10 mCi 177Lu-DTPA-omburtamab
Reporting group description: Intracerebroventricular administration of 10 mCi 177Lu-DTPA-omburtamab for up to two cycles (Part 1).	
Reporting group title	25 mCi 177Lu-DTPA-omburtamab
Reporting group description: Intracerebroventricular administration of 25 mCi 177Lu-DTPA-omburtamab for up to two cycles (Part 1).	

Primary: Dose Limiting Toxicities (DLTs) Part 1

End point title	Dose Limiting Toxicities (DLTs) Part 1 ^[1]
End point description: Summary of DLTs in DLT evaluable subjects.	
End point type	Primary
End point timeframe: Days 1 through 35 in cycle 1	

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: DLTs summarised

End point values	10 mCi 177Lu-DTPA-omburtamab	25 mCi 177Lu-DTPA-omburtamab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	1		
Units: participants	0	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From 1st dose to 5 weeks after last dose, up to 10 weeks (2 cycles).

Assessment type	Systematic
-----------------	------------

Dictionary used

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

Dictionary version	24.1
--------------------	------

Reporting groups

Reporting group title	10 mCi 177Lu-DTPA-omburtamab
-----------------------	------------------------------

Reporting group description:

Intracerebroventricular administration of 10 mCi 177Lu-DTPA-omburtamab for up to two cycles (Part 1).
177Lu-DTPA-omburtamab: Biological, radiolabeled DTPA-omburtamab

Reporting group title	25 mCi 177Lu-DTPA-omburtamab
-----------------------	------------------------------

Reporting group description:

Intracerebroventricular administration of 25 mCi 177Lu-DTPA-omburtamab for up to two cycles (Part 1).
177Lu-DTPA-omburtamab: Biological, radiolabeled DTPA-omburta

Serious adverse events	10 mCi 177Lu-DTPA-omburtamab	25 mCi 177Lu-DTPA-omburtamab	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)	0 / 1 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Partial seizures			
subjects affected / exposed	1 / 1 (100.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	10 mCi 177Lu-DTPA-omburtamab	25 mCi 177Lu-DTPA-omburtamab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	1 / 1 (100.00%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	1	
Blood albumin decreased			

subjects affected / exposed	0 / 1 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	1	
Neutrophil count decreased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	1	
Platelet count decreased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	1	
White blood cell count decreased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 November 2021	<ul style="list-style-type: none">• Section 1.2.1 (Summary of clinical information) updated• Table 1 replaced• 2.2.2.1 & 2.2.2.2: Evaluation timepoints added to the endpoints• Added: Final assessment of the eligibility criteria is done prior to first dose• EOT visit changed to 5-6 weeks after the last dose• Follow-up visits re-scheduled as per first dose• Figure 1 updated• 3.1.1.1 simplified• Adapted description of clinical trials (Trial 03-133 and Trial 101) and the non-clinical summary• The primary endpoint of Part 1 changed to number of DLTs and Part 2 changed to number and severity of TEAEs• Inclusion and exclusion criteria adapted• Follow up changed to every 13 weeks
20 April 2022	<ul style="list-style-type: none">• Allowing a longer screening period• Adapted exclusion criterion #6• Allowing delay in dosing due to logistic reasons• Adapting the sentinel dosing, so that the time frame is until first treatment dose (and not the dosimetry dose).• Removing follow-up period from Part 1• Removing efficacy related objectives and endpoints in Part 1• Removing the analyses of ctDNA & B7-H3 (including the applicable objectives and endpoints)• Schedule of Assessments updated

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
11 August 2022	The trial was terminated after two subjects - due to a business strategy decision	-

Notes:

Limitations and caveats

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

The trial was terminated after 2 subjects due to a business strategy decision. At this point the maximum tolerated dose was not established.

Notes: