



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 ¹⁷⁷ Lu-DTPA-omburtamab | 25 mCi ¹⁷⁷ Lu-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: