Clinical trial results:
An Adaptive, Multicenter, Open-Label Study to Evaluate the Safety, Tolerability, Efficacy, and Pharmacokinetics of Intra-articular AMB-05X Injections in Subjects with Tenosynovial Giant Cell Tumor of the Knee

Summary

EudraCT number	2020-003275-17
Trial protocol	PL NL
Global end of trial date	05 July 2022

Results information

Result version number	v1 (current)
This version publication date	21 May 2023
First version publication date	21 May 2023

Trial information

Trial identification

Sponsor protocol code	AMB-051-01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04731675
WHO universal trial number (UTN)	-
Other trial identifiers	IND: 100835

Notes:

Sponsors

Sponsor organisation name	AmMax Bio, Inc.
Sponsor organisation address	555 Twin Dolphin Drive, Suite 610 , Redwood City,, United States, CA 94065
Public contact	Senior Director, Clinical Operation, AmMax Bio., Inc., +1 (650) 492-9484, tiffanynguyen@ammaxbio.com
Scientific contact	Chief Scientific Officer, AmMax Bio., Inc., +1 (650) 492-9484, kirkjohnson@ammaxbio.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	21 October 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 July 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1. Proportion who achieve an overall tumor response at Week 12
2. Proportion with overall response based on tumor volume score (TVS)
3. Mean change from Baseline in ROM
4. Mean change from Baseline in the PRO Measurement Information System Physical Function score
5. Mean change from Baseline in Worst Stiffness Numeric Rating Scale (NRS) score
6. Percentage who respond with a decrease of at least 30% in mean Brief Pain Inventory score
7. Mean change from Baseline in BPI
8. Mean change from Baseline in Worst Pain NRS score
9. EQ-5D-5L Health Assessment
10. Serum and synovial CSF1 levels
11. Serum and synovial AMB-05X levels
12. Serum and synovial anti-AMB-05X antibody levels

Protection of trial subjects:

Treated in routine care.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 May 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	Ukraine: 1
Country: Number of subjects enrolled	United States: 2
Country: Number of subjects enrolled	Netherlands: 8
Worldwide total number of subjects	11
EEA total number of subjects	8

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)	11
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment was from 2021-04-02 included Netherlands, United States and Ukraine

Pre-assignment

Screening details:

Number of Subjects Screened 19 (100.0%)
Number of Subjects who Failed Screening 8 (42.1%)
Number of Subjects Enrolled 11 (57.9%)
Number of Subjects Dosed 11 (57.9%)

Period 1

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

Arms

Arm title	Single arm study
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	human monoclonal antibody against CSF1R
Investigational medicinal product code	AMB-05X,
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Injection

Dosage and administration details:

The drug product was a sterile, clear, colorless to slightly yellow solution containing drug substance at a concentration of 70 mg/mL. Drug product was packaged in sterile 20-mL glass vials each containing a deliverable volume of 3.0 mL and stored frozen between -20 C and -70 C, protected from light. AMB-05X was administered via IA injection to the affected knee at a dose of either 150 mg or 90 mg drug substance.

Number of subjects in period 1	Single arm study
Started	11
Completed	10
Not completed	1
Lost to follow-up	1

Baseline characteristics

End points

End points reporting groups

Reporting group title	Single arm study
Reporting group description: -	
Subject analysis set title	Test set
Subject analysis set type	Full analysis
Subject analysis set description:	
Safety Efficacy PD/PK	

Primary: frequency and severity of reported TEAEs.

End point title	frequency and severity of reported TEAEs.[1]
End point description:	
End point type	Primary
End point timeframe:	
12 weeks	

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: It is a small single arm study based on descriptive statistics

End point values	Single arm study			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: reported TEAEs	11			

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary endpoint

End point title	Secondary endpoint
End point description:	
1.The proportion of subjects who achieve an overall tumor response (objective response[OR], which includes both complete response [CR] and partial response [PR]), per theResponse Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) (Eisenhauer,2009) at Week 12 2.Proportion of subjects with overall response based on TVS, a TGCT-specific method thatcalculates tumor volume as a percentage of the estimated maximally distended synovialactivity 3.Mean change from Baseline in ROM score 4.Mean change from Baseline in the PROMIS Physical Function score 5.Mean change from Baseline in Worst Stiffness NRS score 6.Percentage of subjects who respond with a decrease of at least 30% in mean BPI score 7.Mean change from Baseline in BPI 8.Mean change from Baseline in Worst Pain NRS score 9.EQ-5D-5L Health Assessment 10.Serum and synovial CSF1 levels 11.Serum and synovial AMB-05X levels 12.Serum and synovial anti-AMB-05X antibody levels	
End point type	Secondary

End point timeframe:
12 weeks

End point values	Single arm study			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: proportion of subjects	11			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: AEs will be recorded from the time the ICF is signed until the subject completes the last study visit or withdraws from the study.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups	
Reporting group title	150 mg AMB-05X
Reporting group description: Subjects who received 150 mg AMB-05X.	
Reporting group title	90 mg AMB-05X
Reporting group description: Subjects receiving subjects in the 90-mg dose	

Serious adverse events	150 mg AMB-05X	90 mg AMB-05X	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 3 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	150 mg AMB-05X	90 mg AMB-05X	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)	0 / 3 (0.00%)	
Vascular disorders			
Edema			
subjects affected / exposed	6 / 8 (75.00%)	0 / 3 (0.00%)	
occurrences (all)	6	0	
Cardiac disorders			
Hypertension			
subjects affected / exposed	3 / 8 (37.50%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Nervous system disorders			

Fatigue subjects affected / exposed occurrences (all)	2 / 8 (25.00%) 2	0 / 3 (0.00%) 0	
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all)	 4 / 8 (50.00%) 4 3 / 8 (37.50%) 3	 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0	
Psychiatric disorders Disturbance in attention subjects affected / exposed occurrences (all)	 2 / 8 (25.00%) 2	 0 / 3 (0.00%) 0	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	 4 / 8 (50.00%) 4	 0 / 3 (0.00%) 0	
Infections and infestations COVID-19 subjects affected / exposed occurrences (all)	 3 / 8 (37.50%) 3	 0 / 3 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 August 2021	Version 2.1: In addition to integrating the country-specific changes made in Version 2.0 for Poland (Section 9.8.1.3) and Version 2.0 for Netherlands (Section 9.8.1.4) into the global protocol, the following major changes were made in global Version 2.1: Exclusion Criterion #2 was revised to allow previous use of pexidartinib, oral tyrosine kinase inhibitors, or any biologic treatment targeting CSF1 or CSF1R >3 months before Baseline. Use of pexidartinib, oral tyrosine kinase inhibitors, or biologic treatment targeting CSF1 or CSF1R within 3 months before Baseline remained exclusionary. Exclusion Criterion #3 was revised to exclude individuals with any history of reconstructive knee surgery in addition to the previously excluded history of extensive knee surgery. In addition, prior diagnostic synovectomy was not to be excluded if it was performed at least 3 months before Baseline, rather than the previous specification of at least 6 months before Baseline. This amendment was implemented after screening and treatment of some subjects had begun.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported