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

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Obtain safety and efficacy data for the investigational drug AMB-05X in the treatment of tenosynovial giant cell tumor (TGCT)

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Synovial and bursal disorders
Study type	Interventional

Summary

ID

NL-OMON50981

Source
ToetsingOnline

Brief title
AMB-05X treatment, into the joint, for patients with TGCT of the knee.

Condition

- Synovial and bursal disorders

Synonym
giant cell tumor in the knee

Research involving
Human

Sponsors and support

Primary sponsor: AmMax Bio Inc
Source(s) of monetary or material Support: Industry

Intervention

Keyword: in-joint treatment, TGCT

Outcome measures

Primary outcome

1. Frequency and severity of reported treatment-emergent adverse events (TEAEs)

Secondary outcome

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 the Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) (Eisenhauer, 2009) at Week 12

2. Proportion of subjects with overall response based on tumor volume score (TVS), a TGCT*specific method that calculates tumor volume as a percentage of the estimated maximally distended synovial activity

3. Mean change from Baseline in range of motion (ROM)

4. Mean change from Baseline in the Patient-Reported Outcomes Measurement Information System (PROMIS) Physical Function score

5. Mean change from Baseline in Worst Stiffness Numeric Rating Scale (NRS) score

6. Percentage of subjects who respond with a decrease of at least 30% in mean Brief Pain Inventory (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

Study description

Background summary

AMB-05X drug substance is a human monoclonal antibody against the colony-stimulating factor 1 receptor (CSF1R). This drug candidate is thought to block the growth-promoting activity in TGCT. Given the limitations of current treatment options, the localized nature of the disease and prior clinical validation of CSF1R as an effective treatment target, AMB-05X is being developed by the sponsor.

Study objective

Obtain safety and efficacy data for the investigational drug AMB-05X in the treatment of tenosynovial giant cell tumor (TGCT)

Study design

This is a multicenter study with an adaptive design that will enroll approximately 12 subjects with TGCT of the knee for 12 weeks of multiple-dose, open-label treatment with AMB-05X.

The study schema is provided in Section 1.2, and the Schedule of Events is provided in Section 1.3 of the protocol.

The study will begin dosing AMB-05X at 150 mg administered via intra-articular injection to the affected knee joint. Subjects will receive an injection of AMB-05X once every 2 weeks for 12 weeks (for 6 treatments total).

Safety, pharmacokinetics (PK), pharmacodynamics (PD), and efficacy assessments will be reviewed by the Sponsor on a continuous, subject-by-subject basis to determine whether the assigned dose is appropriate. Depending on these results, the Sponsor may either decrease the dosage strength to 90 mg or increase the dosage strength to 210 mg in subsequent subjects who enroll. In general,

subjects are expected to complete the study at the dose strength which they started the study, unless they experience a clinically significant AE that would warrant a dose reduction. As a general rule, clinically significant AEs include, but are not limited to, any AE considered to be at least possibly related to study drug and severe in intensity or meets the criteria for a SAE. Subjects who are unable to tolerate a dosage strength of 90 mg will be withdrawn from the study.

When at least 3 subjects have completed Week 6, a data monitoring committee (DMC) will review the available safety, tolerability, PK, PD, and efficacy data. Study enrollment and conduct may continue unchanged during DMC review. Based on the recommendations of the DMC, the Sponsor may then implement any one of the following adaptive changes without a protocol amendment:
* Continuation of enrollment under the existing design, without any changes to the study.
* Continuation of enrollment with a new dose. Specifically, the DMC may recommend a dose reduction to 90 mg or a dose increase to 210 mg in subsequent subjects. Subjects may not exceed a dose of 210 mg or go below a dose of 90 mg. Subjects who are unable to tolerate a dose of 90 mg will be discontinued from the study.
* Discontinuation of further enrollment and/or suspension/termination of the study.
Thereafter, the DMC should continue to review available data on a regular basis throughout the study (each time 3 subjects complete study treatment) and provide ongoing recommendations regarding appropriate next steps in study conduct (as outlined above). If a change in dose is made during the study, the DMC will again review the available data when 3 subjects have completed Week 6 at the new dose and provide further recommendations as outlined above.

Intervention

The Schedule of Events is provided in Section 1.3 of the protocol.

Study burden and risks

The patients will come to the hosptial 10 times, treatment will take place 6 times.

Risks associated with assessments done during these visits:
- Blood collection: Blood will be collected from a vein in the arm during this study. Approximately 65,0 ml of blood (see details in section J) and approximately 12 ml of synovial fluid will be taken at some study visits. Possible side effects or risks from blood collection include swelling of the vein, pain, bruising, or bleeding at the site of collection, feeling faint or dizzy.
- ECG: Skin irritation could occur from the electrodes or gel that is used.

- Questionnaires/Tests of simple tasks: There are no physical risks associated with these questionnaires/tests.
- confidentiallity, however all is done to comply with GDPR.
- common side effects: Fatigue (feeling tired), facial swelling, increases in liver enzyme tests (changes in tests that measure the functioning of your liver), rash, itch, decrease appetite. Because the drug AMB-05X is investigational, there may be other risks that are unknown.
- Sometimes, people have severe allergic reactions to drugs. A severe allergic reaction could be life-threatening and may result in death. Symptoms of possible allergic reactions include rash, difficulty breathing, coughing, wheezing, sudden drop in blood pressure, swelling of the mouth, throat or eyes, seizures, flushing, fainting, a fast pulse and sweating.

AMB-05X may lead to improvement of the disease, but this is not certain.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

1. Subject * 18 years must be able to communicate well with study staff, understand and comply with the requirements of the study, and read and voluntarily sign the ICF prior to the conduct of any study specific procedures.
2. A diagnosis of TGCT of the knee joint, that has been histologically confirmed either by a pathologist at the treating institution or by a central pathologist. If not previously confirmed, biopsy with histological confirmation is required.
3. Measurable disease of at least 1 cm based on RECIST v1.1, assessed from MRI scans by a central radiologist. Subjects with one knee joint involvement only, and only limited posterior extra-articular nodular TGCT lesions as assessed by central radiologist and tumor review committee.
4. Stable prescription of analgesic regimen during the 2 weeks before Baseline
5. Negative urine drug screen (UDS) at Screening and Baseline
6. Women of childbearing potential must have a negative serum pregnancy test at Screening and a negative urine pregnancy test at Baseline.
7. Agrees to follow contraception guidelines (see Section 5.3)
8. Adequate hematologic, hepatic, and renal function, at Screening Visit defined by:
* Absolute neutrophil count * 1.5 × 109/L
* Aspartate aminotransferase or alanine aminotransferase (AST or ALT) * 1.5 × upper limit of normal (ULN)
* Hemoglobin > 10 g/dL
* Total bilirubin * 1.5 × ULN
* Platelet count * 100 × 109/L
* Serum creatinine * 1.5 × ULN
9. Willing and able to complete the Brief Pain Inventory (BPI), Worst Stiffness NRS item, PROMIS Physical Function Scale, EQ-5D-5L, and other self-assessment instruments throughout the study

Exclusion criteria

1. Prior investigational drug use within 4 weeks or 5 half-lives (whichever is longer) before Baseline
2. Previous use of pexidartinib, any biologic treatment targeting CSF1 or CSF1R, or oral tyrosine kinase inhibitors (e.g., imatinib or nilotinib)
3. History of extensive knee surgery except for prior diagnostic synovectomy which is not exclusionary if at least 6 months prior to Baseline
4. Active cancer (either currently or within 1 year before Baseline) that requires therapy (e.g., surgery, chemotherapy, or radiation therapy), with the exception of adequately treated basal or squamous cell carcinoma of the skin, melanoma in situ, carcinoma in situ of the cervix or breast, or

prostate carcinoma not requiring treatment apart from active surveillance.
5. Known metastatic TGCT
6. Hepatitis C virus (HCV) or hepatitis B virus (HBV) or known active or chronic infection with human immunodeficiency virus (HIV)
7. Known active tuberculosis
8. Significant concomitant arthropathy in the affected joint, serious illness, uncontrolled infection, or a medical or psychiatric history that, in the Investigator's opinion, would likely interfere with the subject*s study participation or the interpretation of his or her results
9. Women who are breastfeeding
10. A screening Fridericia-corrected QT interval (QTcF) * 450 ms (men) or * 470 ms (women)
11. MRI contraindications (e.g., pacemaker, loose metallic implants)
12. History of hypersensitivity to any ingredient of the study drug
13. History of drug or alcohol abuse within 3 months before the first dose of study drug
14. Any other severe acute or chronic medical or psychiatric condition or clinically significant laboratory abnormality that may increase the risk associated with study participation/treatment or interfere with interpretation of study results and, in the Investigator*s opinion, make the subject inappropriate for this study
15. Subjects who, in the Investigator*s opinion, should not participate in the study for any reason, including if there is a question about their ability to comply with study requirements

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-05-2021
Enrollment:	10

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	AMB-05X
Generic name:	AMB-05X

Ethics review

Approved WMO Date:	05-01-2021
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	23-02-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	26-03-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	02-04-2021
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	13-09-2021

Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	29-09-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	18-02-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	10-05-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2020-003275-17-NL
CCMO	NL75437.058.20
Other	US IND 151382