A Phase 3 Open-label Extension Study to Assess the Long-term Safety and Efficacy of Intravenous ATB200 Co-administered With Oral AT2221 in Adult Subjects With Late-onset Pompe Disease

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This study has been transitioned to CTIS with ID 2023-505170-15-00 check the CTIS register for the current data. The objective of the study is to assess the long-term safety and efficacy of intravenous ATB200 co-administration with oral AT2221 in...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Musculoskeletal and connective tissue disorders congenital
Study type	Interventional

Summary

ID

NL-OMON54552

Source
ToetsingOnline

Brief title
ATB200-07 Study

Condition

- Musculoskeletal and connective tissue disorders congenital
- Musculoskeletal and connective tissue disorders congenital

Synonym

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Glycogen storage disease type II, Pompe disease

Research involving
Human

Sponsors and support

Primary sponsor: Amicus Therapeutics
Source(s) of monetary or material Support: Amicus Therapeutics;Inc.

Intervention

Keyword: Co-administration, Enzyme Replacement Therapy, Late-onset Pompe Disease, Open-Label Study

Outcome measures

Primary outcome

The long-term safety profile of ATB200/AT2221 will be characterized using

incidence of treatment-emergent adverse events (TEAEs), serious adverse events

(SAEs), and AEs leading to discontinuation of study drug, frequency and

severity of immediate and late IARs, and any abnormalities noted in other

safety assessments (eg, clinical laboratory tests, ECGs, vital signs).

Immunogenicity to ATB200 will also be described.

Secondary outcome

Efficacy endpoints are as follows:

• change from baseline in 6-minute walk distance (6MWD)

• change from baseline in 6MWD (% predicted)

• change from baseline in sitting FVC (% predicted)

• change from baseline in the manual muscle test score for the lower extremities

• change from baseline in the total score for the PROMIS - physical function

• change from baseline in the total score for the PROMIS - fatigue

• change from baseline in the following variables related to motor function:

* GSGC total score

* time to complete the 10-meter walk (ie, assessment of gait) of the GSGC test

* time to complete the 4-stair climb of the GSGC test

* time to complete the Gower*s maneuver of the GSGC test

* time to arise from a chair as part of the GSGC test

* change from baseline in the time to complete the TUG test

• change from baseline in the following variables related to muscle strength:

* manual muscle test score for the upper extremities

* manual muscle test total score (upper and lower extremities combined)

* quantitative muscle test value (kg) for the upper extremities

* quantitative muscle test value (kg) for the lower extremities

* quantitative muscle test total value (kg) (upper and lower extremities combined)

• change from baseline in the following variables from patient-reported outcome measures:

* total score for the PROMIS - dyspnea

* total score for the PROMIS - upper extremity

* R-PAct Scale total score

* EQ-5D-5L health status

• actual value of the subject*s functional status (improving, stable, or declining) pertaining to the effects of study drug in the following areas of life, as measured by the SGIC:

* overall physical well-being

* effort of breathing

* muscle strength

* muscle function

* ability to move around

* activities of daily living

* energy level

* level of muscular pain

• actual value of the subject*s functional status (improving, stable, or declining), as measured by the PGIC

• change from baseline in the following measures of pulmonary function, as follows:

* sitting SVC (% predicted)

* MIP (cmH2O)

* MIP (% predicted)

* MEP (cmH2O)

* MEP (% predicted)

* SNIP (cmH2O)

Pharmacodynamic endpoints are as follows:

• change from baseline in serum CK level

• change from baseline in urinary Hex4 level

Study description

Background summary

Pompe disease is a disease that results in loss of muscle function and strength. This is because patients with Pompe disease are born with a gene

mutation in a specific enzyme. Different genes carry the information that determines different characteristics of people, and this is why there so many different people with different hair and eye colours. In people with Pompe disease there is a mutation in one of these genes and therefore you will develop lower levels of that enzyme causing your muscle to not function properly.

Enzyme replacement therapy has become available for all patients to replace the defected enzyme with *healthy* enzyme. It has been shown that the magnitude and duration of therapeutic response with continuing therapy vary among individual patients. The current therapy, at best, may offer improvements for a limited duration followed by a slow decline of therapeutic effectiveness. The co-administration of ATB200 with AT2221 is designed to address these limitations of current therapy.

Study objective

This study has been transitioned to CTIS with ID 2023-505170-15-00 check the CTIS register for the current data.

The objective of the study is to assess the long-term safety and efficacy of intravenous ATB200 co-administration with oral AT2221 in adult subjects with late-onset Pompe disease.

Study design

This is a multicenter, international open-label extension study of ATB200/AT2221 in adult subjects with late-onset Pompe disease (LOPD) who completed Study ATB200-03.

Intervention

ATB200/AT2221 will be co-administered as follows: AT2221 260 mg (4 × 65-mg oral capsules) for subjects weighing >= 50 kg and 195 mg (3 × 65-mg oral capsules) for subjects weighing >= 40 kg to < 50 kg, followed approximately 1 hour later by ATB200 20 mg/kg (reconstituted lyophilized drug product, 105 mg/vial), administered over a 4-hour intravenous [IV] infusion. The ATB200/AT2221 combination regimen will be administered every 2 weeks. Note: Subjects are required to fast at least 2 hours before and 2 hours after administration of AT2221.

Study burden and risks

ATB200/AT2221 has proven overall to be generally safe and relatively well tolerated. Alternative treatments provide initial benefit to patients with Pompe disease. The magnitude and duration of therapeutic response with

continuing therapy varies among individual subjects and, at best, may offer improvement in measures of muscle function, strength, and respiratory function for a finite duration, ie, 2 to 3 years in most subjects, followed by a slow decline in these parameters. These alternative treatments may themselves be associated with significant risks. A monthly review for safety signals is part of routine pharmacovigilance.

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 must provide signed informed consent prior to any study-related procedures being performed. If the subject is under 20 years of age, the subject must provide written informed consent.
2. Subject must have completed Study ATB200-03.

Note: Subjects who were forced to withdraw from Study ATB200-03 for a logistical reason not related to the efficacy or safety of ATB200/AT2221 (eg, hospitalization for a car accident or emergency surgery) and which resulted in several consecutive missed doses may be eligible to participate in this study upon approval by the Amicus medical monitor.
3. Female subjects of childbearing potential and male subjects must agree to use medically accepted methods of contraception during the study and for 90 days after the last dose of study drug.

Exclusion criteria

1. Subject plans to receive gene therapy or participate in another interventional study for Pompe disease.
2. Subject has a hypersensitivity to any excipients in ATB200 or ATB2221 or medical condition or any other extenuating circumstance that may, in the opinion of the investigator or medical monitor, pose an undue safety risk to the subject or may compromise his/her ability to comply with or adversely impact protocol requirements. This includes clinical depression (as diagnosed by a psychiatrist or other mental health professional) with uncontrolled or poorly controlled symptoms.
3. Subject, if female, is pregnant or breastfeeding.
4. Subject, whether male or female, is planning to conceive a child during the study.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	16-11-2020
Enrollment:	1

Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	AT2221
Generic name:	N-butyl-deoxynojirimycin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	ATB200
Generic name:	recombinant human acid &alfa;-glucosidase (rhGAA)

Ethics review

Approved WMO Date:	22-01-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-04-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-05-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-07-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-09-2020

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-11-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-12-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-11-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-02-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-07-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-07-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-02-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	11-02-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-03-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-07-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-10-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-01-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-03-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
EU-CTR	CTIS2023-505170-15-00
EudraCT	EUCTR2019-000954-67-NL
ClinicalTrials.gov	NCT04138277
CCMO	NL71554.078.20