An Open Label Study to Evaluate the Long-term Safety and Efficacy of Odevixibat (A4250) in Patients with Alagille Syndrome (ASSERT-EXT)

Published: 02-09-2021
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This study has been transitioned to CTIS with ID 2023-509028-17-00 check the CTIS register for the current data. To demonstrate a sustained effect of odevixibat on pruritus in patients with ALGS who have completed study A4250-012 (ASSERT)

Ethical review	Approved WMO
Status	Pending
Health condition type	Hepatobiliary disorders congenital
Study type	Interventional

Summary

ID

NL-OMON54015

Source
ToetsingOnline

Brief title
ASSERT-EXT

Condition

- Hepatobiliary disorders congenital

Synonym
Alagille Syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Albireo AB

Source(s) of monetary or material Support: Albireo AB

Intervention

Keyword: Alagille Syndrome, Assert-EXT, Odevixibat (A4250)

Outcome measures

Primary outcome

Change from baseline in scratching through Week 72 as measured by the Albireo observer-reported outcomes (ObsRO) caregiver instrument

Secondary outcome

• Change in serum bile acid levels from baseline to Week 72

• Change from baseline through Week 72 in patient reported and observer reported itching and scratching severity scores, respectively, for the morning and evening assessments

• Percentage of patients achieving a clinically meaningful decrease in pruritus (pruritus responders) at each visit as measured by the Albireo ObsRO/patient reported outcomes (PRO) instruments

• Change from baseline to Week 72 in sleep parameters as measured with the Albireo ObsRO/PRO instruments (e.g. tiredness and number of awakenings)

• Change from baseline to Week 72 in Pediatric Quality of Life Inventory (PedsQL) scores

• Assessment of Global Symptom Relief from baseline to Weeks 4, 12, 24, 48 and 72 as measured by patient, caregiver, and clinician Global Impression of Symptoms (PGIS, CaGIS, CGIS) items

• Assessment of Global Symptom Relief as measured by patient, caregiver, and clinician Global Impression of Change (PGIC, CaGIC, CGIC) items at Weeks 4, 12,

24, 48, and 72

• Change in serum bile acid levels from baseline through Week 72

Study description

Background summary

In this investigational study, odevixibat is under development for treatment of pruritus in patients with ALGS.
Currently, there is no approved medical therapy for the treatment of pruritus in patients with ALGS. The majority of patients present with severe, intractable pruritus, which can be disabling. Attempts at managing pruritus are made by including ursodeoxycholic acid, cholestyramine, rifampin, ondansetron, or naltrexone in the patient*s treatment regimen; these agents are at best partially effective. Biliary diversion surgery is occasionally used to treat intractable pruritus with some success. Treatment of persistent cholestasis and progressive liver cirrhosis is supportive and usually includes a choleretic agent. Kasai hepatoportoenterostomy (HPE) has been attempted to increase biliary flow from the liver to the intestine, but unlike patients with biliary atresia, those with ALGS who undergo the procedure have a worse outcome . Approximately 15% to 25% of patients with ALGS will require a liver transplant during childhood. For patients with ALGS there is a positive response to transplant with about 90% of patients showing improvement in liver parameters and some degree of catch-up growth. The 5-year survival post-transplant in this population is about 80% .

By inhibiting IBAT with high selectivity and potency, odevixibat has the potential to reduce the elevations in systemic bile acids that result from cholestasis and decrease pruritus, thereby improving the health and wellbeing of patients affected with ALGS. By reducing the elevations in systemic bile acids, odevixibat also has the potential to improve liver function and modify the progression of liver damage in patients with ALGS.

Study objective

This study has been transitioned to CTIS with ID 2023-509028-17-00 check the CTIS register for the current data.

To demonstrate a sustained effect of odevixibat on pruritus in patients with ALGS who have completed study A4250-012 (ASSERT)

Study design

Phase 3, multi-center, open-label extension study

Intervention

Odevixibat (A4250), 120 µg/kg/day once daily, orally administered

Study burden and risks

See schedule of assessments on pages 20-23 of the protocol for more information.
Patient participation in this study will last approximately 76 weeks. During this period, the patient will visit the hospital at least 10 times. The screening visit and the treatment visits last 2 - 6 hours.
During these visits, the following tests and procedures will take place:
- physical examination is performed and questions are asked about medical history.
- weight, height, blood pressure, temperature and heart rate are measured
- blood and urine samples will be taken.
- The study doctor will also perform a pregnancy test on female subjects of childbearing age.
- Subjects are asked to keep an eDiary
Possible side effects that are already known are described in the IB and patient information letter.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)
Babies and toddlers (28 days-23 months)

Inclusion criteria

1. Completion of the 24-week Treatment Period of Study A4250-012;
2. Signed informed consent and assent as appropriate. Patients who turn 18 years of age (or legal age per country) during the study will be required to re-consent to remain on the study;
3. Caregivers (and age-appropriate patients) must be willing and able to use an electronic diary (eDiary) device as required by the study;
4. Sexually active males and females must agree to use a reliable contraceptive method with <= 1% failure rate (such as intra-uterine device, or complete abstinence) from signed informed consent through 90 days after last dose of study drug;

Exclusion criteria

1. Decompensated liver disease, history or presence of clinically significant ascites, variceal hemorrhage, and/or encephalopathy;
2. Patients who were not compliant with study drug treatment or procedures in Study A4250-012;
3. Any other conditions or abnormalities which, in the opinion of the investigator, may compromise the safety of the patient, or interfere with the patient participating in or completing the study;
4. Known hypersensitivity to any components of odevixibat;

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2021
Enrollment:	6
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	TBD
Generic name:	Odevixibat
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	02-09-2021
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	04-03-2022
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-02-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO

Date:	21-06-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	CTIS2023-509028-17-00
EudraCT	EUCTR2021-000996-36-NL
CCMO	NL78174.042.21