An Open-label Multicenter Study to Evaluate the Pharmacokinetics, Pharmacodynamics, and Safety of Inebilizumab in Pediatric Subjects with Neuromyelitis Optica Spectrum Disorder

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This study has been transitioned to CTIS with ID 2023-510007-22-00 check the CTIS register for the current data. NMOSD is associated with a high degree of disability and mortality, and there is a unmet medical need in children with this disease....

Ethical review	Approved WMO
Status	Pending
Health condition type	Spinal cord and nerve root disorders
Study type	Interventional

Summary

ID

NL-OMON53937

Source
ToetsingOnline

Brief title
A study of a new drug in children with NMOSD.

Condition

- Spinal cord and nerve root disorders

Synonym
Spinal cord and optic nerve disorder

Research involving
Human

Sponsors and support

Primary sponsor: Horizon Therapeutics Ireland DAC
Source(s) of monetary or material Support: sponsor

Intervention

Keyword: Inebilizumab, NMOSD, Pediatric

Outcome measures

Primary outcome

Objectives:

1. To characterize the PK of inebilizumab administered in pediatric subjects with NMOSD

2. To characterize the PD of inebilizumab administered in pediatric subjects with NMOSD

3. To assess the safety and tolerability of inebilizumab administered in pediatric subjects with NMOSD

Endpoints:

1. PK parameters, including maximum observed concentration, area under the concentration-time curve from time 0 to 14 days postdose and from time 0 extrapolated to infinity, systemic clearance, terminal elimination half-life, and volume of distribution at steady state

2. Cluster of differentiation 20 positive B-cell counts on Days 1, 8, 15, 29, 57, 85, 113, 155, and 197

3. Safety and tolerability assessments, including incidence of adverse events (AEs), serious AEs, and AEs of special interest, and changes in laboratory parameters and vital signs

Secondary outcome

Objectives:

1. To assess disease activity when inebilizumab is administered in pediatric subjects with NMOSD

2. To assess health-related quality of life (HRQoL) when inebilizumab is administered in pediatric subjects with NMOSD

3. To assess visual acuity when inebilizumab is administered in pediatric subjects with NMOSD

4. To assess disability when inebilizumab is administered in pediatric subjects with NMOSD

5. To characterize the immunogenicity of inebilizumab administered in pediatric subjects with NMOSD

Endpoints:

1. Disease activity endpoints include:

• Time to first relapse

• Proportion of relapse-free subjects

• Annualized relapse rate

2. HRQoL endpoints include:

• Change in Euro Quality of Life-5 Dimension Youth score

• Change in Pediatric Quality of Life Inventory

3. Change in visual acuity

4. Change in Expanded Disability Status Scale

5. Presence of antidrug antibody

Study description

Background summary

Neuromyelitis optica spectrum disorder (NMOSD; also known as Devic*s syndrome and previously known as neuromyelitis optica [NMO]) is a rare, chronic, autoimmune, inflammatory disorder of the central nervous system (CNS), characterized by attacks of predominantly optic neuritis and longitudinally extensive transverse myelitis and, less frequently, affecting the brain and brainstem. Commonly reported symptoms include ocular pain, unilateral or bilateral loss of visual acuity that can reach blindness, loss of sensation, weakness (including paraplegia), bladder and bowel dysfunction, paroxysmal tonic spasms of the trunk and limbs, and Lhermitte*s phenomenon (Wingerchuk et al, 2007). Brain and brainstem involvement are rare, and may cause symptoms such as nausea, intractable vomiting, hiccups, and acute neurogenic respiratory failure (Wingerchuk et al, 1999, Misu et al, 2005). Up to 90% of patients with NMOSD have recurring episodes of optic neuritis and/or myelitis rather than following a monophasic course (Ghezzi et al, 2004, Wingerchuk et al, 1999). Attacks occur within one year of onset in 60% of patients and within 3 years in 90% of patients. Attacks can be severe and result in blindness, paralysis, and even death due to neurogenic respiratory failure (Oh and Levy, 2012). Incomplete recovery from attacks is typical, and accumulative disabilities arise from the severity and frequency of attacks. By some estimates, within 5 years > 50% of adult patients are blind in one or both eyes or require ambulatory assistance (Wingerchuk et al, 2007). Historically, mortality in adults with NMOSD was as high as 30% at 5 years, but a study conducted within the past decade suggests 9% at 6 years (Kitley et al, 2012).

Study objective

This study has been transitioned to CTIS with ID 2023-510007-22-00 check the CTIS register for the current data.

NMOSD is associated with a high degree of disability and mortality, and there is a unmet medical need in children with this disease.
Results from the pivotal study (Study CD-IA-MEDI-551-1155) in adult patients with NMOSD demonstrated a 77% reduction in the risk of developing an NMOSD attack with inebilizumab when compared with placebo in AQP4-IgG seropositive patients after 28 weeks (hazard ratio: 0.227; P < 0.0001), with an acceptable safety profile.
Based on the essential similarity of the clinical features, pathophysiology, diagnostic criteria, treatment responses, and prognosis of AQP4-IgG positive NMOSD in children and adults, inebilizumab treatment may also provide benefit to children with NMOSD. The proposed study aims to collect safety and PK/PD data from subjects < 18 years of age to inform the potential use of

inebilizumab as maintenance treatment in pediatric patients with AQP4-IgG seropositive NMOSD. Specifically, data generated in this study will enable modeling and simulation as part of efficacy extrapolation from the adult NMOSD study (Study CD-IA-MEDI-551-1155). The purpose and design of this study has been discussed and agreed with the European Medicines Agency Pediatric Committee and forms a key commitment as part of the Pediatric Investigation Plan (PIP) for inebilizumab in NMOSD.

1. HRQoL endpoints include:

-Change in Euro Quality of Life-5 Dimension Youth (EQ-5D-Y) score

-Change in Pediatric Quality of Life Inventory (PedsQL)

2. Change in visual acuity

3. Change in EDSS

4. Presence of anti-drug antibody (ADA)

Study design

This is an open-label multicenter study to evaluate the pharmacokinetics (PK), pharmacodynamics (PD), and safety of inebilizumab in eligible pediatric subjects 2 to < 18 years of age with recently active neuromyelitis optica spectrum disorder (NMOSD) who are seropositive for autoantibodies against aquaporin-4 (AQP4 immunoglobulin [Ig]G).
Following a screening period of up to 28 days, a maximum of 15 eligible pediatric subjects will receive inebilizumab on Day 1 and Day 15 of the treatment period; subjects will receive one subsequent dose administered on Day 197 (Week 28). After Day 197 (Week 28), subjects will be followed quarterly for an additional 12 months for safety, PK/PD, and efficacy assessments (through Week 80 [end of study]). Inebilizumab will be used as monotherapy to treat NMOSD, though an initial corticosteroid taper is permitted.
If the Investigator believes the subject would benefit from continued treatment with inebilizumab, the subject will have the opportunity to continue receiving inebilizumab after their participation in the trial (eg, through a Sponsor-supported managed access program). These subjects must complete the Week 52 visit to be eligible to continue treatment and will exit the study following the Week 52 visit. The next dosing for these subjects will be administered in the managed access program 6 months after the last dose of inebilizumab in this study (Day 197) to maintain continuity of treatment.
Safety and other data will be periodically reviewed by an Independent Data Monitoring Committee (IDMC).

Intervention

Inebilizumab administered intravenously (IV) on Days 1, 15, and 197 as follows:
• For subjects weighing <= 37.5 kg: 8 mg/kg IV
• For subjects weighing > 37.5 kg: 300 mg IV fixed dose

Study burden and risks

- Taking a blood sample can be a little painful. Or getting a bruise as a result.
- The study drug will be administered as an infusion. This can cause damage to the skin, irritation of the vein, or damage to the vein.
- there might be side effects from the premedication taken before receiving the study drug.
- Measuring blood pressure might cause some discomfort or bruising to the upper arm.

See also section 6 and 7 and Appendix D in Main ICF

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)

Inclusion criteria

1. Written informed consent and any locally required data privacy authorization obtained from the subject*s legally authorized representative in accordance with regional laws or regulations and the subject*s assent, when applicable, prior to performing any protocol-related procedures.
2. Male or female subjects, minimum body weight of 15 kg, age 2 to <18 years at the time of screening.
3. Positive serum anti-AQP4-IgG result at screening (verified by the central laboratory) and diagnosed with NMOSD.
4. Documented history of one or more NMOSD acute relapses within the last year, or 2 or more NMOSD acute relapses within 2 years prior to screening.
5. Female subjects of childbearing potential who are sexually active with a nonsterilized male partner must agree to use a highly effective method of contraception from screening until 6 months after the final dose of investigational product (IP)
6. Nonsterilized male subjects who are sexually active with a female partner of childbearing potential must agree to use a male condom from Day 1 until 3 months after the final dose of IP.

Exclusion criteria

1. Any condition that, in the opinion of the Investigator, would interfere with the evaluation or administration of the IP or interpretation of subject safety or study results
2. Concurrent/previous enrollment in another clinical study involving an investigational treatment within 4 weeks or 5 published half-lives of the investigational treatment, whichever is the longer, prior to Day 1
3. Females who are breastfeeding, pregnant, or who intend to become pregnant at any time from screening until 6 months after the final dose of IP
4. Known history of allergy or reaction to any component of the IP formulation or history of anaphylaxis following any biologic therapy
5. Evidence of alcohol, drug, or chemical abuse, or a recent history of such abuse <1 year prior to Day 1
6. Major surgery within 8 weeks prior to screening
7. Spontaneous or induced abortion, still or live birth, or pregnancy <= 4 weeks prior to screening
8. Evidence of significant hepatic, renal, or metabolic dysfunction or significant hematological abnormality

9. Receipt of rituximab or any experimental B-cell depleting agent within 6 months prior to screening unless B-cell counts have returned to >= one-half the LLN
10. Receipt of intravenous immunoglobulin (IVIG) within one month prior to Day 1
11. Receipt of particular immunosuppressive therapy within 2 months prior to Day 1
12. Receipt of natalizumab (Tysabri®) within 6 months prior to Day 1
13. Severe drug allergic history or anaphylaxis to 2 or more food products or medicine
14. Diagnosed with a concurrent autoimmune disease that is uncontrolled (unless approved by the medical monitor)
15. Receipt of any of the following:
a. Any live or attenuated vaccine within 4 weeks prior to Day 1
b. Bacillus Calmette-Guérin vaccine within one year of screening
c. Blood transfusion within 4 weeks prior to screening or during screening
16. Clinically significant serious active or chronic viral, bacterial, or fungal infection that requires treatment with anti-infectives, within 2 months prior to Day 1
17. Known history of congenital or acquired immunodeficiency that predisposes the subject to infection
18. Positive test for chronic hepatitis B infection at screening
19. Positive test for hepatitis C virus antibody
20. Negative test for varicella zoster virus (VZV)-IgG
21. History of cancer, apart from squamous cell or basal cell carcinoma of the skin treated with documented success of curative therapy > 3 months prior to Day 1
22. History of active or latent tuberculosis
23. For subjects who may undergo MRI scans: Unable to undergo an MRI scan (eg, hypersensitivity to Gd containing MRI contrast agents, implanted pacemakers, defibrillators, or other metallic objects on or inside the body that limit performing MRI scans), or unable to tolerate or comply with the MRI procedure.

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	28-07-2023
Enrollment:	2
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Inebilizumab
Generic name:	Inebilizumab

Ethics review

Approved WMO Date:	16-02-2023
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-08-2023
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	CTIS2023-510007-22-00
EudraCT	EUCTR2021-003528-33-NL
CCMO	NL83400.100.23