Utilization of the Navigate Anti-AAV9 Antibody Assay in Support of the Novartis* Clinical Studies: COAV101B12301 *STEER* and COAV101B12302 *STRENGTH*

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The primary objective of this study is to evaluate the performance of the Navigate Anti-AAV9 Antibody Assay using serum specimens in subjects with SMA in Novartis clinical studies COAV101B12301 *STEER* and COAV101B12302 *STRENGTH*.

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

Summary

ID

NL-OMON56696

Source
ToetsingOnline

Brief title
Navigate Anti-AAV9 Antibody Assay Performance Study

Condition

- Neuromuscular disorders

Synonym
motor neuron disease, spinal muscular atrophy, Werdnig-Hoffmann disease

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma A.G.

Intervention

Keyword: Analytical Performance validation, Anti-AAV9 antibody Assay, SMA

Outcome measures

Primary outcome

The primary objective of this study is to evaluate the performance of the Navigate Anti-AAV9 Antibody Assay using serum specimens in subjects with SMA in Novartis clinical studies COAV101B12301 *STEER* and COAV101B12302 *STRENGTH*.

The primary measures of performance for the Navigate Assay are linked to the primary and secondary endpoints of Novartis clinical studies COAV101B12301 *STEER* and COAV101B12302 *STRENGTH*:

STEER Primary Objective:

EFFICACY: To compare the efficacy of OAV101 IT vs. sham control as measured by the change from baseline in HFMSE total score

STRENGTH Primary Objective:

To characterize the safety and tolerability of OAV101 IT over a 52-week period in patients with SMA aged 2 to 12 years who have discontinued treatment with nusinersen (Spinraza®) or risdiplam (Evrysdi®).

Secondary outcome

NA

Study description

Background summary

Since OAV101 is a non-replicating recombinant AAV9 virus containing the human SMN complementary deoxyribonucleic acid (cDNA), the presence of anti-AAV9 antibodies in SMA patients should be tested to determine eligibility for treatment with OAV101. Previous exposure to naturally occurring (wild type) AAVs results in preexisting immunity that can potentially compromise transgene expression by blocking transduction. It has been suggested that this could limit therapeutic efficacy and raise potential safety concern (Mendell et al 2022). Immunity developed in seronegative patients after gene transfer may also limit the ability to re-administer treatment if necessary.
According to several clinical studies, (Day et al 2021), patients of various ages express AAV9 antibodies. The incidence of preexisting Abs in the general population tends to increase with age, but not everybody develops anti-AAV Abs. Immunity to AAV is often generated in childhood by the age of 2 years (Calcedo et al 2011). Several studies have reported on the prevalence of anti-AAV9 antibodies in the pediatric population that show low rates of prior exposure to AAV9 (Harrington et al 2016, Fu et al 2017). .

The purpose of this interventional clinical performance study is to establish or confirm aspects of device performance which cannot be determined by analytical performance studies, literature and/or previous experience gained by routine diagnostic testing. This information is used to demonstrate compliance with the relevant general safety and performance requirements with respect to clinical performance. The data obtained shall be used in the performance evaluation process and be part of the clinical evidence for the device.
Novartis currently has two clinical trials for which an investigational clinical trial assay (CTA) developed by Navigate will be used to detect pre-existing anti-AAV9 antibodies in SMA patients (see Intended Purpose above). Novartis has instituted anti-AAV9 antibody testing in prior OAV101 studies in order to exclude patients with antibody titer levels of > 1:50 titer by ELISA. Based on the validation studies performed on the Navigate anti-AAV9 Antibody Assay, a titer of >100 will be used in this assay for exclusion of the patients as this titer correlates to the >1:50 by ELISA.

Study objective

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Study design

There will be one testing site located in the US: Navigate BioPharma Services, Inc., A Novartis Subsidiary conducting the Navigate Anti-AAV9 Antibody Assay. Informed consent regarding diagnostic testing, sample collection for diagnostic testing and patient enrollment are conducted under the drug clinical trials COAV101B12301 *STEER* and COAV101B12302 *STRENGTH*. The conduct of the Navigate Assay testing at Navigate BioPharma is an essential part of the drug clinical trials and is addressed within the protocol and informed consent materials.
Navigate Anti-AAV9 Antibody Assay will be utilized in support of Novartis studies: COAV101B12301 *STEER* and COAV101B12302 *STRENGTH* at a single testing facility in the United States, Navigate BioPharma Services, which is certified by the College of American Pathologists based on Clinical Laboratory Improvement Act.
Specimen testing will be performed in accordance with this protocol and the following assay work instruction, A_WI-10060, Qualitative Determination of Antibodies to Adeno-associated Virus Serotype 9 (AAV9) in Human Serum Using a Bridging Electrochemiluminescent (ECL) Assay.

Intervention

NA

Study burden and risks

NA

Contacts

Public
Novartis

Haaksbergweg 16
Amsterdam 1101 BX
NL
Scientific
Novartis

Haaksbergweg 16
Amsterdam 1101 BX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

STRENGTH Inclusion Criteria
* Written informed consent
* SMA diagnosis based on gene mutation analysis with bi-allelic SMN1 mutations and any copy of SMN2 gene
* Aged 2 < 18 years (screening visit must occur before the patient's 18th birthday) at time of Screening Visit 1
* Have had at least four loading doses of nusinersen (Spinraza®) or at least 3 months of treatment with risdiplam (Evrysdi®) at Screening
* Must be able to sit independently but must never have taken steps independently
* Diagnosed through newborn or neonatal screening or patients clinically diagnosed must have age of clinical symptom onset < 18 months
* Meets age-appropriate institutional criteria for use of anesthesia/sedation
* Female participants who are sexually active or have reached menarche must have a negative pregnancy test at Screening. Those females who are sexually active must also agree to use highly effective methods of contraception.

Exclusion criteria

STRENGTH Exclusion Criteria
* Excluding SMA, any medical condition considered clinically significant
* Positive for human immunodeficiency virus (HIV), hepatitis B or hepatitis
* Anti Adeno Associated Virus Serotype 9 (AAV9) antibody titer using an immunoassay is reported as elevated at Screening (reference to >1:50 or a validated result consistent with being elevated)
* Clinically significant abnormalities in test results during screening period and/or at Baseline
* Platelet count less than the lower limit of normal (LLN), or platelet transfusion within 1 month at Screening Visit 1
* Clinically significant abnormal coagulation panel results at Screening

* Hepatic dysfunction (i.e. alanine aminotransferase (ALT), total bilirubin (TBL), gamma-glutamyl transferase (GGT) or glutamate dehydrogenase (GLDH) > upper limit of normal (ULN) at Screening (with the exception of isolated AST elevation: in the absence of other liver laboratory abnormalities, isolated elevated AST is not considered exclusionary)
* Contraindications for lumbar puncture procedure
* At Baseline (Day-1), participants are excluded if they received:
* nusinersen (Spinraza®) within 4 months at Baseline
* risdiplam (Evrysdi®) within 15 days at Baseline
* Vaccinations 2 weeks prior to administration of OAV101
* Hospitalization for a pulmonary event, or for nutritional support within 2 months prior to Screening or inpatient major surgery planned.
* Presence of the following:
* An active infectious process requiring systemic antiviral or antimicrobial therapy up to 30 days prior to OAV101 administration, or
* An active but untreated viral or bacterial infectious process up to 30 days prior to administration of OAV101, or
* Any febrile illness up to 30 days prior to administration of OAV101
* Requiring invasive ventilation, awake noninvasive ventilation for > 6 hours during a 24-hour period, noninvasive ventilation for >12 hours during a 24-hour period or requiring tracheostomy, at Screening and up to OAV101 administration
* Concomitant use of any of the following medication categories within 90 days prior to administration of OAV101
* Ongoing systemic immunosuppressive therapy (e.g., corticosteroids, cyclosporine, tacrolimus, methotrexate, cyclophosphamide, intravenous immunoglobulin, rituximab), plasmapheresis, immunomodulators (e.g., adalimumab)
* History of hypersensitivity to any of the study treatments or its excipients or drugs of similar chemical classes

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Pending

Start date (anticipated):	10-08-2023
Enrollment:	7
Type:	Anticipated

Medical products/devices used

Generic name:	Navigate Anti-AAV9 Antibody Assay (AM-1085)
Registration:	No

Ethics review

Approved WMO Date:	02-04-2024
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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
Other	2023-A00403-42
CCMO	NL84835.000.23