A Phase 3, Multi-center, Open-label Extension Study to Assess the Safety and Efficacy of Viltolarsen in Ambulant Boys with Duchenne Muscular Dystrophy (DMD)

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This study has been transitioned to CTIS with ID 2023-507146-91-00 check the CTIS register for the current data. Primary Objective:• To evaluate the safety and tolerability of viltolarsen administered intravenously (IV) at weekly doses of 80 mg/kg...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Muscle disorders
Study type	Interventional

Summary

ID

NL-OMON51154

Source
ToetsingOnline

Brief title
NS Pharma - NS-065/NCNP-01-302 - VIL302

Condition

- Muscle disorders

Synonym
DMD, Duchenne Muscular Dystrophy

Research involving
Human

Sponsors and support

Primary sponsor: NS Pharma Inc.
Source(s) of monetary or material Support: Industry

Intervention

Keyword: Ambulant boys, DMD, Extension, Viltolarsen

Outcome measures

Primary outcome

Primary Endpoints:

• Vital signs

• Physical examination

• Clinical laboratory tests: hematology and clinical chemistry, Urinalysis and

Urine cytology

• Antibodies to dystrophin and viltolarsen

• 12-lead electrocardiogram (ECG)

• Renal ultrasound

• Treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs)

Secondary outcome

Secondary Endpoints:

• Time to Stand Test (TTSTAND)

• Time to Run/Walk 10 Meters Test (TTRW)

• Six-minute Walk Test (6MWT)

• North Star Ambulatory Assessment (NSAA)

• Time to Climb 4 Stairs Test (TTCLIMB)

• Quantitative muscle strength measured by hand-held dynamometer (elbow

extension, elbow flexion, knee extension, and knee flexion on the dominant side

only)

Exploratory Endpoints:

• Pediatric Outcome Data Collection Instrument (PODCI)

• Personal Adjustment and Role Skills Scale, 3rd edition (PARS III)

Questionnaire

• Loss of ambulation

Study description

Background summary

DMD is a disorder of progressive weakness leading to severe disability and ultimately death. Patients with DMD have mutations in dystrophin, a key muscle protein. For making proteins our body uses a template (mRNA). DMD mutations disrupt this template, leading to incorrect or no protein assembly with as result a deficiency of the dystrophin protein. At present, glucocorticoid (GC) medication is the only treatment that has been shown to slow the decline of strength and function in DMD patients, however, this treatment can have significant side effects. New therapies based on specific genetic makeups are in development. Viltolarsen is designed to interact with the template used for making the dystrophin protein and to correct for the errors introduced by these mutations. The purpose of this study is to investigate how safe and effective the new medicine viltolarsen is for the treatment of DMD.

Study objective

This study has been transitioned to CTIS with ID 2023-507146-91-00 check the CTIS register for the current data.

Primary Objective:
• To evaluate the safety and tolerability of viltolarsen administered intravenously (IV) at weekly doses of 80 mg/kg in boys who have completed the NS 065/NCNP 01-301 study.

Secondary Objective:

• To compare the efficacy of viltolarsen administered IV at weekly doses of 80 mg/kg in boys who have completed the NS 065/NCNP 01-301 study over a 96-week treatment period versus natural history controls using strength and endurance outcomes.

Exploratory Objectives:
• To evaluate health-related quality of life impact of viltolarsen treatment on patient's DMD.
• To evaluate preservation of ambulation of patients with DMD.

Study design

This Phase 3 study is a multi-center, open-label extension study in ambulant boys with DMD who have completed the 48 week treatment period of either viltolarsen or placebo in Study NS 065/NCNP-01-301. Patients will receive viltolarsen administered IV at weekly doses of 80 mg/kg. Study NS-065/NCNP-01-302 will be comprised of a 96-week treatment period.

Intervention

Patients will receive IV infusions of viltolarsen injection administered once weekly over a 96-week period. Patients will be dosed at 80 mg/kg/week.

Study burden and risks

Burden:
Participants have to visit the research center approximately 97 times, over a period of 98 weeks. During each visit participants will receive the study drug via infusion and additional medical test will be done. Some visits can take up to 4 hours. (see section E4 and E6).

Risks and side effects related to the study drug and risks associated with other study procedures.
The most common side effects of the study medicine (vitolarsen) are listed below Diastolic blood pressure increased (5%), Changes in kidney function (43%), Immune/allergic symptoms including rash and joint pain (7%), Impaired ability of the heart to adequately pump blood through the body (7%), Infections (48%). Cancer risk of Viltolarsen is unknown and is currently being investigated in animal experiments. The potential risk in humans, however, cannot be excluded at the present time. The study medicine may cause also side effects that are unknown.

Risks of receiving an infusion: A rash or pain at the site of the infusion, infection can also happen at the infusion site including redness, swelling, and fever. Standard of care procedures for infusions will be followed to minimize any risk of infusion specific related side effects.

Risks of port placement: The risks of the surgery to have the port placed include bruising, scarring, prolonged bleeding from the operation site and infection. Port placement will require anaesthesia. Additional risks of having a port include clots forming in the port, failure of the port device so that it needs to be removed or replaced, introduction of air between the lungs and the chest wall such that the lungs collapse, and injury to a major blood vessel. As with any surgery, there may be other unexpected risks or complications of this surgery that are uncommon but serious, including death.

Risks of port use: The risks include infections, clots forming in the port or in his vein (for example the vein that carries blood to his heart), a change in position of the port so that it no longer works well or failure of the port device so that it needs to be removed or replaced. Infection can become a serious complication that in rare cases can lead to sepsis, shock, and/or death. You and your child will be trained in the proper use and care of a port to reduce these risks and to watch for any problems.

Risks of anaesthesia in DMD: As DMD affects the muscles, patients with DMD have an increased risk of breathing distress from anaesthesia. General anaesthesia may have increased risks including heart complications and death from general anaesthesia. The study doctor will provide special instructions to the surgeon performing the port placement, the selection of anaesthesia will be discussed with you, and all steps to reduce risks will be taken.

Risks of blood sample collection: Risks associated with drawing blood from his arm include momentary discomfort and/or bruising. Infection, excess bleeding, and/or fainting are also possible, although unlikely. Rarely, a more serious injury, such as bleeding under the skin (hematoma) may develop. To reduce discomfort a local numbing cream may be applied. The side effects that may be associated with the numbing cream include lack of sensation to the area where the cream is applied

Renal Ultrasound Risks: There are no known risks. Discomfort is uncommon, but your child will feel some pressure, and may need to drink extra fluids to have a full bladder. Sometimes, an ultrasound may not be able to obtain the pictures your study doctor needs, so other imaging tests may have to be obtained.

Risk of electrocardiography: This test may cause irritation to the skin where the electrodes are placed.

Risks of strength and function tests: It is possible that these tests could make your child more tired than after a regular (non-research) doctor*s visit. There is also a small risk of falling, shortness of breath, or muscle soreness.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

1. Patient has completed the NS-065/NCNP-01-301 study;
2. Patient*s parent(s) or legal guardian(s) has (have) provided written informed consent and Health Insurance Portability and Accountability Act authorization, where applicable, prior to any study-related procedures; patients will be asked to give written or verbal assent according to local requirements;
3. Patient and parent(s)/guardian(s) are willing and able to comply with scheduled visits, investigational product (IP) administration plan, and study procedures.

Exclusion criteria

1. Patient had an adverse event in Study NS 065/NCNP 01 301 that, in the opinion of the investigator and/or the sponsor, precludes safe use of viltolarsen for the patient in this study;
2. Patient had a treatment which was made for the purpose of dystrophin or dystrophin-related protein induction after completion of Study NS-065/NCNP-01-301.
3. Patient took any other investigational drug(s) during or after completion of Study NS-065/NCNP-01-301.
4. Patient is judged by the investigator and/or the sponsor not to be appropriate to participate in the extension study for any reason.

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):	24-09-2021
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Viltolarsen
Generic name:	Viltolarsen

Ethics review

Approved WMO Date:	02-04-2021
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	30-06-2021
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	03-09-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	25-11-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	01-12-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	07-09-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	14-09-2022
Application type:	Amendment
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
EU-CTR	CTIS2023-507146-91-00
EudraCT	EUCTR2021-000122-10-NL
ClinicalTrials.gov	NCT04060199
CCMO	NL76990.000.21