A Multicenter, Double-blind, Placebo-controlled, Phase 1 Study of WVE-210201 Administered Intravenously to Patients with Duchenne Muscular Dystrophy

Published: 27-02-2018
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Primary objective:Evaluate the safety and tolerability of single ascending doses of WVE-210201 in patients with DMD. Secondary objective:Assess the pharmacokinetics (PK) of WVE-210201 in patients with DMD.

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

Summary

ID

NL-OMON46461

Source
ToetsingOnline

Brief title
WVE-DMDX51-01

Condition

- Musculoskeletal and connective tissue disorders congenital

Synonym
DMD, Duchenne Muscular Dystrophy

Research involving
Human

Sponsors and support

Primary sponsor: Wave Life Sciences Ltd.

Source(s) of monetary or material Support: industry;sponsor

Intervention

Keyword: DMD, Duchenne Muscular Dystrophy

Outcome measures

Primary outcome

Primary objective:

Evaluate the safety and tolerability of single ascending doses of WVE-210201 in

patients with DMD.

Secondary outcome

Secondary objective:

Assess the pharmacokinetics (PK) of WVE-210201 in patients with DMD.

Study description

Background summary

This research study is testing a new investigational medicine called *WVE-210201.* *Investigational* means that the medicine is still being tested and has not been approved for sale by the United States (US) Food and Drug Administration (FDA), the European Medicines Agency (EMA) or similar government agencies abroad and can only be used in clinical studies.

The primary objective of this study is to evaluate the safety and tolerability of a single infusion of WVE-210201.

Study objective

Primary objective:
Evaluate the safety and tolerability of single ascending doses of WVE-210201 in patients with DMD.
Secondary objective:
Assess the pharmacokinetics (PK) of WVE-210201 in patients with DMD.

Study design

Patients enrolled in this study will be enrolled in 1 of 4 dose groups. The group into which your child is enrolled depends on which group is open when your child enters the study. Patients in the first group will receive the lowest dose of WVE-210201 or placebo and patients in the fourth group will receive the highest dose of WVE-210201 or placebo.

If at least 8 patients have been given study drug at 1 dose and that dose level is considered safe and acceptable, the next group of patients who are enrolled will be assigned to a higher dose level. This will continue until the highest planned dose level has been studied or until it is no longer considered safe to test a higher dose level.

Intervention

The study will include a Screening Visit, a Dosing Visit, and Follow-up for approximately 12 weeks (through Day 85 [±3 days]).

Screening evaluations must be conducted within 28 days prior to the Baseline visit. Written informed consent (and minor assent when applicable) will be obtained from the patient*s parent or legal guardian (and the patient as applicable) prior to participation in this study.
Four dose levels are planned to be administered in this study. Each cohort will have 8 patients, 6 receiving WVE 210201 and 2 receiving placebo. Eligible patients will be randomized (6:2) to 1 of 4 dose cohorts described below:
* Cohort 1: 1 mg/kg
* Cohort 2: 2 mg/kg
* Cohort 3: 5 mg/kg
* Cohort 4: 10 mg/kg
Within each cohort, study drug will be administered as a single intravenous (IV) dose on Day 1. Patients will undergo predose and postdose safety assessments and PK blood sampling. Dosing will be initiated in a staggered manner, in which 2 sentinel patients (1 placebo and 1 active) will be dosed and observed for safety in the clinic for 48 hours. If either patient experiences a serious adverse event (SAE), the Safety Monitoring Committee (SMC) will review the safety data and determine if it is safe to proceed with the cohort. If neither patient experiences an SAE during that period, the remaining 6 patients (5 WVE-210201 and 1 placebo) will be dosed in a sequential fashion, dosing occurring at least 24 hours apart. Non-sentinel patients will remain in the clinic for 24 hours of follow-up. Additional follow-up safety assessments will be performed weekly until Day 29 and monthly afterwards for a total of approximately 12 weeks (through Day 85 [±3 days]). PK sampling will be performed on Day 1, Day 2, and Day 8.
Dosing of the cohorts will be sequential, starting at the lowest dose level; thus, Cohort 1 will be enrolled and all patients will complete single dose administration and a follow-up of a minimum of 14 -days (ie, complete the Day 15 Visit) prior to safety data review by the Dose Escalation Committee (DEC)

and approval by the chairperson of the SMC to enable initiation of Cohort 2, and so forth.

Study burden and risks

zie schedule of event in protocol.

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Risks of the WVE-210201:
WVE-210201 has not been studied in humans yet. Therefore there is no information about the safety of WVE-210201 in humans and the risks are not known. In studies in animals (mice and monkeys) given WVE-210201, the drug was well tolerated at doses up to those planned for this study.

WVE-210201 is a type of drug called an antisense oligonucleotide. Based on what we know about other similar drugs, there may be a risk of potential damage

to your liver or kidneys, changes in your blood (a decrease in platelets which are involved in clotting and an increase in the time it takes for your blood to clot) and changes in your immune reactions that can cause inflammation. At doses much higher than what will be used in this study, some mice had damage to their liver after treatment with WVE-210201. These risks will be monitored closely throughout the study.

Risks of blood collection
Your child may experience pain and discomfort at the site where the needle enters the skin. There is a slight risk of fainting, bruising or swelling. On rare occasions, an infection may develop at the site where the needle enters the skin.

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. Patient and/or parent or legal guardian must have the ability and be willing to provide written informed consent prior to any study-related procedures.
2. Diagnosis of DMD based on clinical phenotype with increased serum creatine kinase.
3. Documented mutation in the dystrophin gene associated with DMD that is amenable to exon 51 skipping.
4. Ambulatory or non-ambulatory male.
5. Age of *5 and *18 years at randomization
tests, study restrictions, and all study procedures.
7. Stable pulmonary and cardiac function, documented within the past year, as measured by:
a) Reproducible percent predicted forced vital capacity (FVC) *50%
b) Left ventricular ejection fraction (LVEF) >55% in patients <10 years of age and >45% in patients *10 years of age, as measured (and documented) by echocardiogram.
8. Sexually mature males must be willing to use contraception for the duration of the study, if the patient is sexually active.
9. Patiënten en verzorgers moeten ermee instemmen geen studiegerelateerde informatie op sociale media te plaatsen

Exclusion criteria

1. Clinically significant medical finding on the physical examination other than DMD that, in the judgment of the Investigator will make the patient unsuitable for participation in, and/or unable to complete the study procedures.
2. Other prior or ongoing medical conditions including:
a. Acute illness within 28 days of Screening visit;
b. Abnormal physical findings, other than those associated with musculoskeletal findings attributable to DMD.
3. Laboratory abnormality, that, in the Investigator's opinion, could adversely affect the safety of the patient, make it unlikely that the course of treatment or follow up would be completed, or impair the assessment of study results. These include, but are not limited to:
a. Renal insufficiency;
b. Impaired hepatic function (alanine aminotransferase
c. [ALT] and aspartate aminotransferase [AST] elevations inconsistent with age and creatine kinase [CK] level, and elevated direct or indirect bilirubin);
d. Activated partial thromboplastin time [aPTT] values above the upper limit of normal [ULN];
e. Platelet count 4. Positive hepatitis B surface antigen or hepatitis C antibody test.
5. Known to be positive for human immunodeficiency virus (HIV).
6. Severe mental retardation and/or behavioral problems that, in the opinion of the Investigator, could prohibit participation in this study.
7. Severe cardiomyopathy that, in the opinion of the Investigator, prohibits participation in this study. Cardiomyopathy that is managed by angiotensin-converting enzyme (ACE) inhibitors or beta blockers is acceptable provided the patient meets the LVEF inclusion criteria.

8. Need for mechanical or non-invasive ventilation OR anticipated need for mechanical or non-invasive ventilation within the next year, in the opinion of the Investigator.
9. Changes in nutritional or herbal supplements or concomitant medications within 1 month prior to Screening visit or plans to modify (dose or regimen) during the study.
10. Currently on anticoagulants or antithrombotics.
11. Received prior treatment with drisapersen.
12. Received treatment with eteplirsen or ataluren within the past 14 weeks.
13. Received any investigational drug within the past 3 months or 5 half-lives, whichever is longer.
14. Known hypersensitivity to any oligonucleotide, as demonstrated by a systemic allergic reaction such as changes in pulse, blood pressure, breathing function, etc.
15. Parent or legal guardian is directly or indirectly involved in the conduct and administration of this study as an Investigator, sub-investigator, study coordinator, or other study staff member, or the patient is a first-degree family member, significant other, or relative residing with one of the above persons involved directly or indirectly in the study.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-11-2018
Enrollment:	4
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	WVE-210201

Generic name:	WVE-210201

Ethics review

Approved WMO Date:	27-02-2018
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	26-06-2018
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	02-07-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	07-08-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	10-09-2018
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
EudraCT	EUCTR2017-002686-21-NL
CCMO	NL64303.000.18

Study results

Results posted: 14-04-2020

First publication
01-01-1900

URL result
Type
ext
Naam
www.clinicaltrialsregister.eu
URL