WVE - N531

An Open-label Phase 1b/2a Study of WVE-N531 in Patients With Duchenne Muscular Dystrophy

Hub Summary

This is a phase 1b/2a looking at the safety of a new exon skipping investigational therapy, WVE-N531. Wave will also be looking at the pharmacokinetics (how the drug is absorbed and metabolised in the body) and pharmacodynamics (how the drug affects the body).

Only patients who have a mutation amenable to exon 53 skipping are able to participate.

Over the course of the trial, they will look to find the best dose of the investigational therapy, so patients will receive up to 4 dose levels, 4 weeks apart over the course of 16 weeks, and then receive an additional 3 doses every other week.

Study Number: NCT04906460

Description by Wave Life Sciences

This is an initial clinical trial to evaluate the investigational therapy WVE-N531 in boys with Duchenne muscular dystrophy amenable to exon 53 skipping. It is a Phase 1b/2a open-label study, meaning all participants and investigators will know that the drug is being administered. This clinical trial is not placebo-controlled, meaning there will be no dummy treatment.

The objectives of the trial are to evaluate the safety, tolerability, pharmacokinetics (PK) - how the drug is absorbed and metabolized by the body, and pharmacodynamics (PD) - how the drug affects the body, by assessing any changes in dystrophin levels in muscles and any clinical effects.

WVE-N531 is an investigational antisense oligonucleotide (ASO) designed for potential treatment of boys with Duchenne muscular dystrophy amenable to exon 53 skipping. WVE-N531 is given by intravenous (IV) administration.

Over the course of the trial, we will look to find the best dose regimen of the drug. The trial will include a total of approximately 15 participants. An initial cohort will receive ascending doses of WVE-N531. Up to 4 dose levels (administered ≥4 weeks apart) will be evaluated in order to select a dose level for further multiple dose evaluation. The initial patients will receive up to 3 additional doses every other week at that dose level. Additional patients will then be enrolled and dosed every other week at that level. All patients will receive a maximum of 7 total doses followed by a minimum 8-week safety monitoring period.

Primary Outcome Measures

1. Safety: Proportion of patients with adverse events (AEs)

Secondary Outcome Measures

1. Pharmacokinetics: Concentration of WVE-N531 in muscle tissue
2. Pharmacodynamics: Dystrophin level (% normal dystrophin) as assessed by Western blot of muscle tissue following multiple doses of WVE-N531

Can I take part?

Inclusion Criteria

- Diagnosis of DMD based on clinical phenotype with increased serum creatine kinase.
- Documented mutation in the DMD gene associated with DMD that is amenable to exon 53 intervention
- Score of ≥1 on item 1 or 2 of the shoulder component of the Performance of the Upper Limb (PUL).

Trial Status
Fully recruited

UK Locations
Oxford, Fully recruited

Trial Sponsor
Wave Life Sciences

Age
5-18

Mutation Specific
Mutation specific therapies, Exon 53

Muscle Biopsy
Muscle Biopsy Required

MRI
No

Phase
1b/2a

Length Of Participation
22 weeks

Recruitment Target
15

Ambulatory
Ambulant and non-ambulant

Therapeutic Category
Exon Skipping

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- Stable pulmonary and cardiac function, as measured by the following:
  - Reproducible percent predicted forced vital capacity (FVC) ≥50%;
  - 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 (ECHO) or cardiac magnetic resonance imaging (MRI), within 6 months prior to enrollment into the study.
- Adequate deltoid muscle at Screening to perform open muscle biopsies.
- Currently on a stable corticosteroid therapy regimen, defined as initiation of systemic corticosteroid therapy that occurred ≥6 months prior to Screening and no changes in dose ≤3 months prior to Screening visit.

Exclusion Criteria

- Cardiac insufficiency:
  - Severe cardiomyopathy that, in the opinion of the Investigator, prohibits participation in this study; however, cardiomyopathy that is managed by angiotensin-converting-enzyme (ACE) inhibitors or beta blockers is acceptable provided the participant meets the LVEF inclusion criterion.
  - Any other evidence of clinically significant structural or functional heart abnormality.
- Need for daytime mechanical or noninvasive ventilation OR anticipated need for daytime mechanical or noninvasive ventilation within the next year in the opinion of the Investigator. Nighttime noninvasive ventilation is permitted.
- Received prior treatment with an investigational peptide-conjugated phosphorodiamidate morpholino oligomer (PPMO) or drisapersen.
- Received prior treatment with gene therapy for DMD.
- Received treatment with ataluren, viltolarsen, eteplirsen, or golodirsen within the 14 weeks prior to Screening.
- Received any investigational drug within 3 months or 5 half-lives, whichever is longer prior to Screening.

For contact details and to find out more, please refer to dmdhub.org.

Duchenne UK

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