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A phase II proof of concept study to evaluate the efficacy and safety of daxdilimab in participants with dermatomyositis (DM) or anti-synthetase inflammatory myositis (ASIM)

Submission date
06/04/2023

Recruitment status
No longer recruiting

Registration date
04/10/2023

Overall study status
Ongoing

Last Edited
04/10/2023

Condition category
Skin and Connective Tissue Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
This is a randomised double-blind placebo-controlled study in participants with inadequately controlled dermatomyositis (DM) or anti synthetase inflammatory myositis (ASIM).
Myositis is a group of rare conditions affecting the muscles and, in some cases, other body parts like skin, lungs, or heart. It is caused by the body's own defense system attacking the muscle, which causes them to be weak, tired, and swollen. Patients are often in pain, feel unwell, and may have skin or lung complications.
This study is being done to know how well a drug called daxdilimab works and how safe it is in participants with DM or ASIM for whom the usual treatment does not seem to work. This study also aims to describe over time how the body reacts to daxdilimab and how the drug is taken up, broken down, and removed from the body.
Daxdilimab is a protein designed to recognise and attach to a cell involved in the origin and development of conditions, like myositis, where the immune system attacks normal tissue. It is believed that by attaching to these cells, daxdilimab could reduce their number, and in this way reduce the activity of the immune system and help in the potential treatment of these conditions.

Who can participate?
Adults aged 18 - 75 years, with inadequately controlled dermatomyositis (DM) or anti synthetase inflammatory myositis (ASIM).

What does the study involve?
This study consists of a 4 week screening period, 48 week treatment period and a 8 week safety follow up period. Maximum duration 60 weeks.
Up to 96 participants will be randomised in a 1:1 ratio to receive daxdilimab or placebo.
At Week 24, participants who received placebo will receive the study drug, while those who received the study drug will continue with the same dose. Therefore, from Week 24 to Week 44, all participants will receive daxdilimab.

Study drug or placebo will be administered once every 4 weeks by 2 injections under the skin. Study procedures include vital signs, questionnaires, ECGs, blood, and urine samples, and optional MRI.

What are the possible benefits and risks of participating?
By participating in this study, you may or may not see an improvement in your condition and quality of life. Your condition may get better, stay the same, or get worse. You may benefit from the medical monitoring (for example, physical exam and lab tests) that is part of the study. The information from this study may help the Sponsor's understanding of the safety of daxdilimab and its potential effectiveness in participants with dermatomyositis or anti-synthetase inflammatory myositis. This may contribute to the advancement of knowledge in the field of dermatology and rheumatology. Your participation in this research may not benefit you but may benefit future patients with dermatomyositis or anti-synthetase inflammatory myositis regardless of whether daxdilimab is proven to be successful in treating these diseases or not.

Where is the study run from?
Horizon Therapeutics Ireland DAC (United States)

When is the study starting and how long is it expected to run for?
April 2023 to March 2026

Who is funding the study?
Horizon Therapeutics Ireland DAC (United States)

Who is the main contact?
Dr Caroline Cotton, caroline.cotton@liverpoolft.nhs.uk

Contact information

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Scientific

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Additional identifiers

EudraCT/CTIS number
2022-502810-10-00

IRAS number
1006956

ClinicalTrials.gov number
NCT05669014

Secondary identifying numbers
HZNP-DAX-205, IRAS 1006956

Study information

Scientific Title
A phase II, randomized, double-blind, placebo-controlled efficacy and safety study of daxdilimab subcutaneous injection in adult participants with inadequately controlled dermatomyositis or anti-synthetase inflammatory myositis

Study objectives
Primary objective:
To evaluate the effect of daxdilimab compared with placebo in reducing disease activity at Week 24.

Secondary objectives:
1. To evaluate the effect of daxdilimab compared with placebo in reducing disease activity at Week 24.
2. To evaluate the effect of daxdilimab compared with placebo on skin symptoms at Week 24.
3. To evaluate the effect of daxdilimab on decreasing the use of corticosteroid at Week 24.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 02/10/2023, South Central - Hampshire B Research Ethics Committee (2 Redman Place, Stratford, London , E20 1JQ, United Kingdom; +44 (0)207 1048 088; hampshireb.rec@hra.nhs.uk), ref: 23/SC/0138

Study design
Interventional double-blind randomized placebo-controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Diagnostic, Treatment, Safety, Efficacy

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Dermatomyositis (DM) or anti-synthetase inflammatory myositis (ASIM)

Interventions
-Daxdilimab will be administered by subcutaneous (SC) injection every 4 weeks over a total of 44 weeks.
-Matching placebo will be administered by SC injection every 4 weeks over a total of 24 weeks, then will be administered active drug by SC injection up to Week 44

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacokinetic, Pharmacodynamic, Dose response, Pharmacogenetic, Therapy, Prophylaxis

Phase
Phase II

Drug/device/biological/vaccine name(s)
Daxdilimab (also known as HZN-7734, VIB7734 and MEDI7734)

Primary outcome measure
Total improvement score (TIS) at week 24

Secondary outcome measures
1. Proportion of participants with improvement of TIS ≥ 40 and without deterioration at 2 consecutive visits at 24 weeks.
2. Proportion of participants with improvement of TIS ≥ 20 and without deterioration at 2 consecutive visits at 24 weeks.
3. Change in the cutaneous dermatomyositis disease area and severity index (CDASI) activity score from Baseline (Day 1) to Week 24.
4. Proportion of participants on an oral corticosteroid (OCS) dose ≥10 of prednisone or equivalent at Baseline who achieve a clinically meaningful reduction in the OCS dose: either a 25% decrease or an OCS dose of 7.5 mg/day of prednisone or equivalent at Week 24.

5. Serum concentration of daxdilimab (DAX) over time.
6. Prevalence at Baseline and incidence and titer of antidrug antibodies directed against dax over time.
7. Incidence of treatment emergent adverse events (TEAEs)
8. Incidence of treatment emergent serious adverse events (TESAEs)
9. Incidence of TEAESIs: hypersensitivity reaction, including anaphylaxis, herpes zoster infection, severe (CTCAE (Common terminology criteria for adverse events) Grade 3 or higher) viral infection/reactivation, opportunistic infection, and malignancy (except non-melanoma skin cancer).

Overall study start date
04/04/2023

Completion date
15/03/2026

Eligibility

Key inclusion criteria
1. Adult men or women 18 and ≤ 75 years of age at the time of signing the informed consent (ICF).
2. A diagnosis of definite or probable myositis according to American College of Rheumatology /European League Against Rheumatism 2017 (ACR/EULAR 2017) criteria:
2.1. Population 1: DM
2.1.1. Diagnosis of DM with DM rash current or historical, or
2.2. Population 2: ASIM
2.2.1. Anti-histidyl tRNA synthetase-(Anti-Jo-1) antibodies must be positive during screening by central laboratory testing, or
2.2.2. One of following antibodies must be positive by historical testing: directed against anti-alanyl- (anti-PL-12), anti-threonyl-(anti PL-7), anti-asparaginyl-(anti-KS), anti-glycyl-(anti-EJ), anti-isoleucyl-(anti-OJ), anti-phenylalanyl-transfer RNA synthetase-(anti-ZO), anti-tyrosil-YRS(HA).
3. Currently active myositis with all the following (a, b, and c) during screening:
3.1. Manual Muscle Testing (MMT 8) score < 142
3.2. At least 2 other abnormal core set measures (CSM) from the following list:
3.2.1. Patient global disease activity (PtGDA) ≥ 2cm in a 10 cm visual analog scale (VAS)
3.2.2. Physician's Global Disease Activity (PhGDA) ≥ 2 cm in a 10 cm VAS
3.2.3. Extramuscular activity ≥ 2cm in a 10 cm VAS
3.2.4. At least one muscle enzyme 1.5 times upper limit of normal (ULN)
3.2.5. Health assessment questionnaire-disability index (HAQ-DI) ≥ 0.5
3.3. Global muscle damage score ≤ 5 on a 10 cm VAS on the myositis damage index (MDI).
4. Participants should be on stable standard of care therapy if tolerated; if they are not able to tolerate it or have failed standard of care, medications should have a washed out period.
5. Participants should be willing to taper corticosteroid dose per protocol when stable or improving.

Participant type(s)
Patient

Age group
Mixed

Lower age limit
18 Years

Upper age limit
75 Years

Sex
Both

Target number of participants
96

Key exclusion criteria
1. Any condition that, in the opinion of the investigator or sponsor, would interfere with the evaluation of investigational product (IP) or interpretation of participant safety or study results.
2. Weight > 160 kg (352 pounds) at screening.
3. Breastfeeding or pregnant women or women who intend to become pregnant anytime from signing the ICF through 6 months after receiving the last dose of IP.
4. History of clinically meaningful cardiac disease including unstable angina, myocardial infarction, congestive heart failure within 6 months prior to randomization; arrhythmia requiring active therapy, except for clinically insignificant extra systoles, or minor conduction abnormalities; or presence of clinically meaningful abnormality on electrocardiogram (ECG) if, in the opinion of the Investigator, it would increase the risk of study participation.
5. History of cancer within the past 5 years, except as follows:
5.1. In situ carcinoma of the cervix treated with apparent success with curative therapy > 12 months prior to screening, or
5.2. Cutaneous basal cell or squamous cell carcinoma treated with curative therapy.
6. Any underlying condition that in the opinion of the Investigator significantly predisposes the participant to infection.
7. Known history of a primary immunodeficiency or an underlying condition, such as known human immunodeficiency virus (HIV) infection, or a positive result for HIV infection per central laboratory.
8. Confirmed positive test for hepatitis B virus serology as defined in the protocol.
9. Active tuberculosis (TB), or a positive interferon gamma (IFN-γ) release assay (IGRA) test at screening, unless documented history of appropriate treatment for active or latent TB according to local guidelines.
10. Any severe herpes virus family infection (including Epstein-Barr virus, cytomegalovirus [CMV]) at any time prior to randomization.
11. Opportunistic infection requiring hospitalization or parenteral antimicrobial treatment within 2 years prior to randomization.
12. Significant organ system involvement or myositis damage (global muscle damage score > 5 on a 10cm VAS scale on the MDI) that poses risks in the study or impedes assessments.
13. Diagnosis of immune-mediated necrotizing myopathy (IMNM) [(positive 3-hydroxy-3-methylglutaryl-coenzyme A reductase (anti-HMGR), anti-signal recognition particle (anti- SRP), or antibody negative)], inclusion body myositis (IBM) (including positive anti-cytosolic 5'-nucleotidase 1A (anti cN1A), or drug-induced myositis.
14. Current musculoskeletal, joint, or inflammatory disease, including significant joint contractures or calcinosis that in the opinion of the investigator, could interfere with the muscle strength assessments and confound the disease activity assessments.
15. Wheelchair bound participants.
16. Current inflammatory skin disease other than DM or ASIM that, in the opinion of the

investigator, could interfere with the inflammatory skin assessments or confound the disease activity assessments.
17. Severe interstitial lung disease where respiratory symptoms limit participant function or progressive pulmonary fibrosis.
18. Myositis in overlap with another connective tissue disease that precludes the accurate assessment of a treatment response (for example, difficulty in assessing muscle strength in a scleroderma patient with associated myositis).

Date of first enrolment
25/10/2023

Date of final enrolment
18/02/2025

Locations

Countries of recruitment
Argentina

Australia

Brazil

Czech Republic

France

Germany

Italy

Mexico

Spain

United States of America

Study participating centre
University Hospital Aintree
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Study participating centre
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Sponsor information

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Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
Horizon Therapeutics Ireland DAC (United States)

Results and Publications

Publication and dissemination plan
Submission to regulatory authorities
The sponsor, PPD, part of Thermo Fisher Scientific and regulatory authorities will be granted direct access to medical records for verification of study procedures and data without violation confidentiality of the records to the extent permitted by the applicable laws and regulations. Before data transfer all identifiable information will be replaced by a code. The sponsor shall ensure that necessary measures are taken to protect and maintain confidentiality of data when transferred outside of the UK and EEA.

Intention to publish date
15/03/2027

Individual participant data (IPD) sharing plan

The current data sharing plans for this study are unknown and will be available at a later date

IPD sharing plan summary

Data sharing statement to be made available at a later date