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Efficacy and safety of DMX-200 in patients with focal segmental glomerulosclerosis

Submission date
05/02/2022

Recruitment status
No longer recruiting

Registration date
07/07/2022

Overall study status
Ongoing

Last Edited
01/11/2023

Condition category
Urological and Genital Diseases

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

Plain English Summary
Background and study aims
Focal segmental glomerulosclerosis (FSGS) is an injury of the filtering part of the kidneys (glomerulus). It is a progressive kidney disease where the filters (glomeruli) of the kidneys become more ‘leaky’ and allow protein from the blood to collect in the urine (proteinuria). The kidneys' ability to clean the blood is impaired which can lead to kidney failure. FSGS is routinely treated with a type of drug called an angiotensin II receptor blocker (ARB). The aim of this study is to assess the safety and effectiveness of a new drug called DMX-200 (repagermanium) in adult patients with FSGS who are being treated with an ARB. DMX-200 is designed to inhibit the inflammatory response of chronic disease, including FSGS, when given alongside an ARB. This study will investigate to see if the study drug, DMX-200 (repagermanium), reduces the amount of proteinuria and slows the decline of kidney function when taken with an ARB.

Who can participate?
Patients between the ages of 18 to 80 years old with FSGS

What does the study involve?
The study consists of five periods:
1. Screening period (up to 4 weeks), to check that participants qualify for the study.
2. Titration period (up to 4 weeks), required for participants who are not already receiving an ARB treatment at the maximum tolerated dose.
3. Stabilisation period (6 weeks), to check participants remain eligible.
4. Double-blind treatment period (104 weeks), where all participants will be randomly assigned to receive either the study drug or placebo (50/50 chance). A placebo looks like a medicine but does not have any medicine in it.
5. Follow-up period (4 weeks), for post-treatment safety investigations.

What are the possible benefits and risks of participating?
The study medication DMX-200 (repagermanium) and propagermanium (an alternative crystal form of repagermanium) have both been available as nutritional and dietary supplements since the 1970s in Japan and in other countries including the USA and Australia since the 1980s. The use of repagermanium as a dietary supplement is often provided at doses of over 1000 mg/day and human studies have used doses up to 4.0 g/day with no observed negative effects.

Based on published data with propagermanium (Serocion®) at a dose of 30 mg daily in 2,015 patients with hepatitis B, the most frequent adverse events were elevated aspartate aminotransferase (AST), elevated alanine aminotransferase (ALT), general languor, and diminished appetite. In this population, a major adverse reaction of acute exacerbation of chronic hepatitis B has been observed.
Based on clinical data to date, DMX-200 administered at daily doses from 30 to 240 mg for a total duration of up to 28 weeks was found to be safe and well tolerated, and no safety signals were observed. Treatment-associated reduction in proteinuria in patients with FSGS may translate into a long-term nephroprotective (kidney protective) effect. DMX-200 (repagermanium) has been designed to reduce proteinuria and slow the rate of decline of kidney function. The antiproteinuric effect of DMX-200 in patients with FSGS was observed in the DMX-200-202 study. The current study will provide additional and essential long-term effectiveness data to determine the durability of the antiproteinuric effect of DMX-200 over time, as well as its ability to slow the progression of FSGS, as measured by change in estimated glomerular filtration rate (eGFR) compared with placebo. There is no guarantee that patients will benefit from taking part in this study. However, the information obtained in this study may help in the treatment of future patients with FSGS.
This clinical study protocol has been designed such that the risk to patients in this study will be minimised by adequate selection of eligibility criteria, and schedule of clinical monitoring, administration, and treatment duration. The sponsor will immediately notify the Investigator if any information that might materially influence the benefit/risk assessment of DMX-200 becomes available during the study.

Where is the study run from?
Dimerix Bioscience Pty Ltd (Australia)

When is the study starting and how long is it expected to run for?
January 2022 to June 2026

Who is funding the study?
Dimerix Bioscience Pty Ltd (Australia)

Who is the main contact?
Dr Ashish Soman, ACTION3@dimerix.com

Contact information

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Additional identifiers

EudraCT/CTIS number
2021-004174-64

IRAS number
1004525

ClinicalTrials.gov number
NCT05183646

Secondary identifying numbers
DMX-200-301, IRAS 1004525, CPMS 50927

Study information

Scientific Title
A pivotal Phase III, multicenter, randomized, double-blind, placebo-controlled study of the efficacy and safety of DMX-200 in patients with focal segmental glomerulosclerosis (FSGS) who are receiving an angiotensin II receptor blocker (ARB)

Acronym

ACTION3

Study hypothesis
1. To evaluate the efficacy of DMX-200 in terms of urine PCR and eGFR slope in patients with focal segmental glomerulosclerosis (FSGS) who are receiving an angiotensin II receptor blocker (ARB)
2. To evaluate the safety and tolerability of treatment with DMX-200 in patients with FSGS who are receiving an ARB
3. To evaluate the effect of DMX-200 on kidney function parameters including proteinuria in patients with FSGS who are receiving an ARB

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 08/03/2022, Fast-Track Research Ethics Committee (Health Research Authority, 2 Redman Place, Stratford, London, E20 1JQ, UK; Tel: not available; fasttrack.rec@hra.nhs.uk), ref: 22/FT/0027

Study design
Randomized placebo-controlled double-blind trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

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

Condition
Focal segmental glomerulosclerosis

Interventions
Patients will receive either DMX-200 as 120 mg capsules taken orally twice daily (BID) or matching placebo capsules twice daily (BID), over a treatment period of up to 104 weeks. Patients will continue on a stable dose of angiotensin II receptor blocker (ARB) at the maximal tolerated dose and ≥50% of the maximum recommended dose as per the product label throughout the study as prescribed per standard of care. Post-treatment, there will be a 4-week follow-up period and patients will perform their final assessments at the End of Study (EOS) visit at week 108. Randomisation will be performed using an interactive response technology (IRT) system based on a predefined randomisation schedule. A randomisation blocking scheme (1:1 ratio) will be used to ensure that the balance between the treatment groups is maintained.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
DMX-200

Primary outcome measure
1. Treatment efficacy measured by the percentage change in urine protein creatinine ratio (PCR) (based on 24-hour urine collection) from baseline to week 35 following treatment with DMX-200 compared with placebo' after treatment
2. Treatment efficacy measured by the slope of estimated glomerular filtration rate (eGFR) from baseline to week 104 following treatment with DMX-200 compared with placebo' after treatment

Secondary outcome measures
1. Safety and tolerability of treatment measured by the incidence and severity of adverse events (AEs) throughout the study duration
2. Safety and tolerability of treatment with DMX-200, measured by the incidence of clinically significant changes in the safety profile of patients treated with DMX-200 compared with placebo, measured by changes in clinical laboratory evaluations (haematology, coagulation, clinical chemistry, and urinalysis), ECGs, vital signs, and physical examinations from baseline until EOS
3. Kidney function parameters measured by the proportion of responders and non-responders throughout the study duration, defined as:
3.1. Complete response: 24-hour urine PCR reduction to <0.3 g/g (<33.9 mg/mmol)
3.2. Modified partial remission (FPRE): 24-hour urine PCR reduction ≥40% from baseline and <1.5 g/g (<169.5 mg/mmol)
3.3. No response (failure to meet any response criteria)
4. Kidney function parameters measured by the proportion of patients that meet a composite endpoint of worsening in kidney function throughout the study duration, as defined by:
4.1. The onset of kidney failure (initiation of chronic dialysis, kidney transplantation, or sustained eGFR of <15 ml/min/1.73 m²)
4.2. A 30% decline in eGFR from baseline
4.3. Death from kidney or cardiovascular causes

Overall study start date
25/01/2022

Overall study end date
29/06/2026

Eligibility

Participant inclusion criteria
1. A diagnosis of FSGS confirmed by kidney biopsy. NOTE: The biopsy can have been obtained at any time. Diagnosis of FSGS should be based on light microscopy with supportive findings on either electron microscopy or immunofluorescence analysis (preferably both) and the clinical

history and disease course consistent with primary FSGS, genetic FSGS, or FSGS of undetermined cause
2. Must be receiving a stable dose of an ARB (irbesartan, losartan, valsartan, candesartan, olmesartan medoxomil, or azilsartan medoxomil) at the maximal tolerated dose and ≥50% of the maximum recommended dose per the product label for 6 weeks prior to Screening, or willing to transition to this treatment during the Titration and Stabilization period
3. If taking corticosteroids, the dosage must be stable for ≥4 weeks prior to Screening and during the Stabilization period, and patients must have no plan to change their treatment regimen during the study
4. If taking aldosterone inhibitors, mineralocorticoid receptor antagonists, direct renin inhibitors, or sodium-glucose co-transporter-2 inhibitors, the dose and regimen must be stable for ≥26 weeks prior to Screening and during the Stabilization period and patients must have no plan to change their treatment regimen during the study
5. Urine protein/creatinine ratio (PCR) >1.5 g/g (>169.5 mg/mmol) or 24-hour total protein >1.5 g /day based on 24-hour urine collection during Screening
6. Estimated glomerular filtration rate (eGFR) ≥30 ml/min/1.73 m² at Screening and ≥25 mL/min /1.73 m² at the Qualification visit (Week -1)
7. Seated blood pressure ≤160/100 mmHg (mean of 3 values) at Screening and ≤140/90 mmHg (mean of three values) at the Qualification visit (Week -1)
8. Body mass index ≤40 kg/m² at Screening

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
286

Participant exclusion criteria
1. Has FSGS secondary to another condition.- History of type 1 diabetes mellitus, or uncontrolled type 2 diabetes mellitus (defined as glycated hemoglobin >8%), or non-fasting blood glucose >10 mmol/l at Screening
2. History of lymphoma, leukemia, or any active malignancy within the past 2 years (except for basal cell or squamous cell carcinomas of the skin or cervical carcinoma in situ that have been resected and with no evidence of metastatic disease)
3. History of jaundice, active hepatitis, or known hepatobiliary disease (except asymptomatic cholelithiasis)
4. Documented history of heart failure (New York Heart Association Class III/IV) or a major adverse cardiac event within 12 weeks prior to Screening
5. Serum potassium levels >5.5 mmol/l at Screening
6. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) >2 × upper limit of normal at Screening
7. Treatment with immunosuppressant biological drugs, calcineurin inhibitors, cyclophosphamide, azathioprine, or mycophenolate mofetil within 26 weeks prior to Screening
8. Patients with <80.0% compliance to ARB treatment during the Stabilization Period (Weeks -6 to -1) of the study, as confirmed at the Qualification visit

Recruitment start date
23/02/2022

Recruitment end date
15/03/2025

Locations

Countries of recruitment
Argentina

Australia

Brazil

Denmark

England

France

Hong Kong

New Zealand

Scotland

Spain

Taiwan

United Kingdom

United States of America

Study participating centre
Salford Care Organisation
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-

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Funder(s)

Funder type
Industry

Funder Name
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Results and Publications

Publication and dissemination plan
1. Peer-reviewed scientific journals
2. Internal report
3. Conference presentation
4. Publication on website

It is intended that after completion of the study, the data are to be submitted for publication in a scientific journal and/or for reporting at a scientific meeting. The sponsor will post the results of the study in a publicly accessible database in accordance with the applicable laws. No identifiable personal information will be present in any published data. A clinical study report will be prepared for the study and provided to the regulatory agencies in each country, where appropriate.

Intention to publish date
01/08/2026

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository. The study datasets will be stored on an IQVIA network drive. A ticket should be raised with IT to obtain access to the folder. Data type = EDC output in SAS (CRF

extract). Datasets are generated as per request from the Biostatistician team. A programmer will place the datasets at the required location/folder (on a network drive) for a Biostatistician to review. The datasets would be used for the analysis of the study endpoints.

IPD sharing plan summary

Stored in non-publicly available repository