NIHR | Innovation Observatory

Newcastle University

Health Technology Briefing
January 2024

DMX-200 for treating focal segmental glomerulosclerosis in people receiving angiotensin II receptor blocker therapy

Company/Developer	Dimerix Bioscience Pty Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 26875	NICE TSID: Not available	UKPS ID: Not available

Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

DMX-200 is currently in clinical development for treating focal segmental glomerulosclerosis (FSGS) among patients who are also receiving an angiotensin II receptor blocker (ARB). FSGS is a rare disease in which scar tissue develops on the parts of the kidneys that filter waste from the blood (glomeruli). When the glomeruli become damaged or scarred, proteins begin leaking into the urine (proteinuria). Symptoms of FSGS include swelling in body parts, such as legs, ankles and around the eyes (oedema), weight gain, and foamy urine caused by proteins in the urine. However, many people with FSGS do not experience symptoms. If proteinuria remains elevated and kidney function continues to decline, patients progress to end stage kidney disease and require dialysis or kidney transplant. There remains a need for novel and improved treatments for FSGS.

DMX-200 is used concomitantly in patients already receiving an ARB. It inhibits FSGS-associated receptors to reduce proteinuria and is administered orally. If licensed, DMX-200 will offer an additional treatment option for patients with FSGS.

Proposed Indication

Treatment of adults and paediatrics with focal segmental glomerulosclerosis (FSGS) who are receiving a stable dose of an angiotensin II receptor blocker (ARB).[a]

Technology

Description

DMX-200 (repagermanium) works as a chemokine receptor 2 (CCR2) pathway blocker and is administered to patients already taking an angiotensin II type I receptor blocker (ARB).[1] CCR2 is expressed by podocytes, which play a key role in the pathologies of FSGS. DMX-200 is an indirect CCR2 antagonist that targets enzymes associated with CCR2.[2]

DMX-200 is currently in clinical development for the treatment of FSGS among patients who are also receiving an ARB. In the phase III clinical trial (NCT05183646), patients are administered DMX-200 a single 120mg capsule or placebo capsule twice daily for 104 weeks.[3]

Key Innovation

There is a need for novel and improved treatments for FSGS as existing treatments achieved limited success and treatment failure remains common. Prior clinical studies have shown that simultaneous administration of CCR2 antagonists and an ARB could result in reduced proteinuria (high level of protein in urine) and slow down progression of kidney failure.[1,2]

If licensed, DMX-200 will offer an additional treatment option for patients with FSGS.

Regulatory & Development Status

DMX-200 does not currently have marketing authorisation in the EU/UK for any indication.

DMX-200 has been awarded the following regulatory designations:

- an orphan drug in the EU in November 2018 for the treatment of FSGS.[4]
- an Innovation Passport and the Innovative Licensing and Access Pathway (ILAP) in June 2021 from the UK Medicines and Healthcare products Regulatory Agency (MHRA) for FSGS.[5]

Patient Group

Disease Area and Clinical Need

FSGS is a rare disease in which scar tissue develops on the parts of the kidneys that filter waste from the blood (glomeruli).[6] When the glomeruli becomes damaged or scarred (sclerosis), proteins begin leaking into the urine (proteinuria). There are several types of FSGS, such as primary FSGS which is of unknown cause (FSGS-UC); secondary FSGS which is caused by known factors such as infection, drug toxicity, diseases such as diabetes or sickle cell disease, obesity, and other kidney diseases; and genetic (or familial) FSGS which is a rare form of FSGS caused by genetic mutations and is suspected when several members of a family show signs of FSGS. It can also occur when neither parent has the disease, but each carry one copy of an abnormal gene that can be passed on to the next generation.[7] Race, ethnicity, and gender all have a significant effect on the incidence of FSGS.[8] It is more common in people of African ancestry, both children

[a] Information provided by Dimerix Bioscience Ltd

and adults, and affects men slightly more than women. FSGS occurs most often in adults approximately 45 years or older.[8,9] Symptoms of FSGS include swelling in body parts, such as legs, ankles and around the eyes (oedema); weight gain; foamy urine caused by proteins in the urine; high fat levels in the blood (high cholesterol); and low levels of protein in the blood (hypoalbuminemia).[10] However, many people with FSGS do not experience symptoms.[10] Many observational studies have shown that reduction of proteinuria and the achievement of remission are associated with improved kidney outcomes, and resistance to corticosteroids is strongly associated with the risk of kidney failure in adult patients with primary FSGS.

FSGS is estimated to affect about 7 people per million in the general population, although specific incidence rates vary in different populations. It accounts for about 40% of adults with nephrotic syndrome and about 20% of children with nephrotic syndrome.[9] In patients who do not achieve remission, 5-year and 10-year kidney survival was reported to be 60% to 90% and 25% to 56%, respectively.[7] Clinical surveys from the UK and North America have reported the incidence of nephrotic syndrome to be between two and four new cases per 100,000 children per year, with biopsy-confirmed FSGS comprising 15–20% of the total. In a series of 1,368 renal biopsies from patients over 60 years of age, FSGS was present in 5.4% of those patients with nephrotic syndrome.[11] In England, 2021-22, there were 935 finished consultant episodes (FCE) and 747 admissions for nephrotic syndrome with focal and segmental glomerular lesions (ICD-10 code N04.1), which resulted in 1,958 FCE bed days and 535 day cases.[12]

Recommended Treatment Options

NICE recommends the following for the treatment of FSGS:[13]

- Treatment with a corticosteroid such as prednisolone is recommended for the initial episode of FSGS.
- For adults with FSGS, calcineurin inhibitors can be considered as alternatives for those with relative contraindications or intolerance to corticosteroids.
- Ciclosporin is recommended for steroid-resistant FSGS.
- Combination treatment with mycophenolate mofetil and high-dose dexamethasone is recommended for people with steroid-resistant FSGS who are intolerant to ciclosporin.

Clinical Trial Information

Trial	NCT03649152; A Phase 2a, Double-Blind, Randomized, Placebo-Controlled, Crossover Study Evaluating the Safety and Efficacy of Propagermanium in Patients with Primary Focal Segmental Glomerulosclerosis (FSGS) Who Are Receiving Irbesartan **Phase II:** Completed **Location(s):** Australia **Primary completion date:** June 2020
Trial Design	Randomised, crossover assignment, double blind
Population	N=8 (actual); adults 18 to 80 years old; diagnosis of FSGS confirmed by renal biopsy and receiving a stable dose of 300 mg daily dose of irbesartan (in any marketed formulation) for at least 3 months prior to screening, and have no plan to change treatment regime throughout the study
Intervention(s)	DMX-200 one capsule orally twice daily for 16 weeks

Comparator(s)	Placebo
Outcome(s)	The primary outcome was the Number of Adverse Events with the Adjunct use of Propagermanium Compared to Placebo in Participants with FSGS who are Receiving Irbesartan [Time Frame: Sixteen weeks] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Clinical Trial Information

Trial	NCT05183646; A Pivotal Phase 3, 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) **Phase III:** Recruiting **Location(s):** 3 EU countries, UK, USA, and other countries **Primary completion date:** June 2024
Trial Design	Randomised, parallel assignment, double blind
Population	N=286 (estimated); patients 12 to 80 years old; diagnosis of FSGS confirmed by kidney biopsy or documentation of a genetic mutation in a podocyte protein associated with FSGS and receiving an ARB at the maximal tolerated dose or willing to transition
Intervention(s)	DMX-200 120mg capsules twice daily during treatment period (104 weeks)
Comparator(s)	Placebo
Outcome(s)	Primary outcomes: • Efficacy of DMX-200 in terms of urine PCR in patients with FSGS who are receiving an ARB [Time Frame: Baseline to Week 35] • Efficacy of DMX-200 in terms of eGFR slope in patients with FSGS who are receiving an ARB (Analysis at week 35 and Week 104) [Time Frame: Baseline to Week 104] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of DMX-200 is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Sparsentan for treating focal segmental glomerulosclerosis in people 8 years and over (ID3955). Expected date of issue to be confirmed.

NHS England (Policy/Commissioning) Guidance

- NHS England. Clinical Commissioning Policy Statement: Rituximab for the treatment of refractory Focal Segmental Glomerulosclerosis in the native kidney in adults (1818). July 2019.

Other Guidance

- Kidney Disease Improving Global Outcomes (KDIGO). Clinical Practice Guideline for Management of Glomerular Diseases. 2021.[7]
- NHS University Hospitals of Leicester: Nephrotic Syndrome Children's Guideline. 2021.[14]

Additional Information

Dimerix Bioscience Pty Ltd did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

References

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