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ACTION3 pivotal Phase 3 & open-label extension study assessing DMX-200 in adult & paediatric patients with focal segmental glomerulosclerosis (FSGS)

Dimerix

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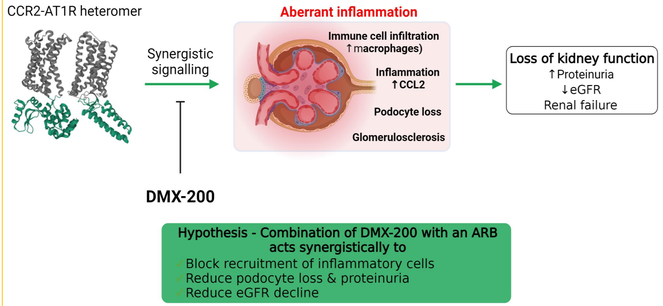
INTRODUCTION

FSGS is a podocytopathy with complications including nephrotic syndrome and progressive kidney failure and is an area of high unmet medical need with very few effective therapeutic options. Dimerix are developing DMX-200 (repagermanium) as an orally active small molecule inhibitor of the chemokine receptor 2 (CCR2). ACTION3 is a global Phase 3 study designed to confirm the proteinuria lowering effects of DMX-200 and assess effects on GFR decline.



AIM

Primary study objective

To evaluate the efficacy of DMX-200 in terms of uPCR and eGFR slope in patients with FSGS receiving an ARB

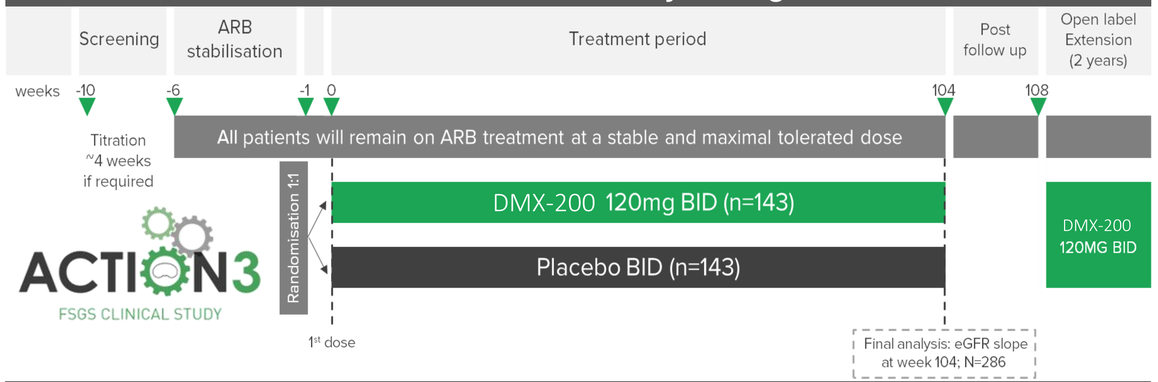
Secondary

To evaluate the safety and tolerability of treatment with DMX-200 in patients with FSGS receiving an ARB

To evaluate the effect of DMX-200 on kidney function parameters including proteinuria in patients with FSGS receiving an ARB

METHOD

ACTION3 - FSGS Pivotal Study Design & Schema



Key Eligibility Criteria and Endpoints

Key Inclusion Criteria

- Age 12 – 80 years
- Biopsy-confirmed FSGS within 7 years
- Receiving a stable dose of ARB at the maximal tolerated dose If taking corticosteroids, dosage must be stable for ≥ 4 weeks prior to screening
- If on aldosterone or direct renin inhibitor, MRA or SGLT2 inhibitor, dose must be stable for 3 months
- Urine PCR >1.5 g/g or 24-hr total protein >1.5 g/d
- Estimated GFR ≥ 25 and <120 mL/min/1.73 m^2
- BP ≤ 160/100 mm Hg
- BMI ≤ 40 kg/m^2

Key Exclusion Criteria

- Secondary FSGS
- Treatment with biological immunosuppressant drugs, CNIs, cyclophosphamide, azathioprine, or mycophenolate mofetil < 12 weeks prior to screening

Primary Endpoint

- Percent change in uPCR from baseline to week 35 with DMX-200 vs placebo.
- Change in eGFR slope from baseline to week 104 with DMX-200 vs placebo.

CONCLUSIONS

In March 2024, an Independent Data Monitoring Committee (IDMC) conduced a futility analysis on data from the first n=72 randomized patients to complete approximately 35 weeks of treatment.

- ACTION3 passed the futility analysis based on a proteinuria efficacy endpoint
- No safety concerns were noted. DMX-200 continues to be very well tolerated with the longest exposure now ~18 months
- ACTION3 is now formally expanding to 185 sites and will now include paediatric patients 12-17 years

RESULTS

Baseline demographics and characteristics	
Patients enrolled (March 2024)	92
Age	44 median (range 18-78)
Gender	62 (67%) Male 30 (33%) Female
Ethnicity	13 (14.1%) Asian 7 (7.6%) Black 67 (72.8%) White 5 (5.4%) Other
FSGS Diagnosis	75 (78.3%) Primary 10 (10.9%) Genetic 9 (9.8%) Undetermined 1 (1.1%) Other
Concomitant SGLT2-inhibitor use	15 (16.3%)
uPCR (g/g)	3.28 ± 2.38
eGFR mL/min/1.73 m^2	57.7 ± 27.6
BMI (kg/m^2) (median)	25.59 (range 17.68-38.08)
Time since diagnosis months	54.8 ± 66.60
eGFR ml/min/1.73 m^2	
≥ 90 ml/min/1.73 m^2	14 (15.2%)
≥ 60 to <90 ml/min/1.73 m^2	21 (22.8%)
≥ 45 to <60 ml/min/1.73 m^2	17 (18.4%)
≥ 30 to <45 ml/min/1.73 m^2	31 (33.7%)
<30 ml/min/1.73 m^2	9 (9.8%)
uPCR (g/g) by pre-defined strata; n (%)	
≤3.5 g/g uPCR & eGFR ≥ 25 to <60 ml/min/1.73 m^2	1.93 ± 0.23 (26%)
≤3.5 g/g uPCR & eGFR >60 ml/min/1.73 m^2	2.20 ± 0.94 (39%)
>3.5 g/g uPCR & ≥ 25 to <60 ml/min/1.73 m^2	6.03 ± 2.81 (26%)
>3.5 g/g uPCR & eGFR >60 ml/min/1.73 m^2	4.38 ± 1.18 (9%)

CONTACT INFORMATION

ClinicalTrials.gov Identifier
NCT05183646

For further information
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REFERENCES

1. Ayoub, M., et al. (2015). PLOS ONE, e0119803