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P381 -Randomised Controlled Trial Protocol: The Use of Rituximab In the treatment of Nephrotic Glomerulonephritis (TURING)

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RESEARCH QUESTION
TURING is a two-arm, placebo controlled, double blind Phase III study designed to address the question: Does the addition of rituximab to standard of care delay relapse in patients with Minimal Change Disease (MCD) and nephrotic Focal Segmental Glomerulosclerosis (FSGS)?

SETTING
TURING was developed by the Renal Association Glomerulonephritis Clinical Study Group with patient representation and is funded by the NIHR. This trial is in the process of regulatory and ethics submissions and is planned to open for recruitment at around 30 UK Renal Units in the second quarter of 2019.

BACKGROUND
MCD and FSGS are rare diseases that cause nephrosis. Patients suffer with debilitating oedema, and are at increased risk of infection and venous thromboembolism. Standard of care consists of high dose glucocorticoids, with associated morbidity including weight gain, diabetes, infection and osteoporosis. Patients require frequent hospital visits, hence these diseases carry a high socioeconomic burden. This is particularly high in FSGS, where patients with uncontrolled disease progress to end stage kidney disease (ESKD), and may develop recurrent disease post transplantation. Better treatments are needed for MCD/FSGS.
Rituximab is a monoclonal B cell depleting antibody, which is licensed for other autoimmune diseases, including ANCA vasculitis, another cause of ESKD. Rituximab delays relapse in children with relapsing MCD/FSGS, but due to a lack of randomised controlled trial data, is not funded by NHSE for adults.

AIMS AND OBJECTIVES
Primary objective: to assess the effect of rituximab on time from remission to relapse in patients with MCD/FSGS.
Secondary objectives: to assess the effect of rituximab on (i) NHS and societal resource use and hence cost to assess the effect of rituximab on safety and on secondary measures of efficacy (ii) Health status

METHODS
112 patients with newly presenting or relapsing nephrotic MCD/FSGS will be recruited. They will be randomised to receive rituximab (2 x 1g within 4 weeks of randomisation, followed by 1g at 6 months) or placebo. All patients will receive standard of care treatment with prednisolone, with a protocolised dosing regimen. Trial follow up visits will align with routine clinic visits. Data collection will include proteinuria, serum albumin, renal function and a health status questionnaire (EQ5D). The primary endpoint will be time from partial/complete remission to relapse. The study is powered with a 5% significance level, at least 80% power to detect a 50% change in median time to relapse between the two arms when a minimum of 67 primary endpoint events are observed, which is expected 24 months after the last patient recruited. An

open label extension phase will be offered to patients in the placebo arm who relapse having previously achieved at least a partial remission. These patients may then receive rituximab according to the protocol. All patients will be recruited to the National Registry of Rare Disease (RaDaR) to facilitate long term follow up, and will be invited to enrol in the National Study of Nephrotic Syndrome (NephroS) for collection of biological samples, including DNA.