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The use of rituximab in the treatment of nephrotic glomerulonephritis

Submission date
17/06/2019

Recruitment status
No longer recruiting

Registration date
21/06/2019

Overall study status
Ongoing

Last Edited
14/01/2026

Condition category
Urological and Genital Diseases

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

Plain English summary of protocol

Background and study aims
Minimal change disease (MCD) and focal segmental glomerulosclerosis (FSGS) are rare autoimmune kidney diseases that lead the patient to develop nephrotic syndrome and if untreated can result in substantial morbidity, including kidney failure and death. All the current treatments have serious limitations and glucocorticoids are the mainstay of treatment in MCD /FSGS. Although they are effective in most of the patients, recurrent relapses happen in 75% of the patients when the steroid dose is reduced or withdrawn. Frequent relapses result in high cumulative steroid exposure, which in turn increases the risk of obesity, diabetes, infection and osteoporosis.
There is a critical need for steroid alternative treatments in MCD/FSG patients that are both effective and safe, and do not adversely affect kidney function. Rituximab is the most promising candidate treatment. It is currently a licensed treatment for other autoimmune diseases, where it has an excellent safety profile. Moreover, randomised trial evidence already supports the use of rituximab in children with MCD/FSGS. This study, TURING, will assess if giving rituximab to an adult patient with nephrotic syndrome caused by MCD/FSGS is safe, effective in preventing relapses of the disease and determine how long patients remain well. TURING will help doctors to decide the best course of treatment for future patients.

Who can participate?
Aged 16 or older who have new or relapsing nephrotic syndrome as a consequence of minimal change disease (MCD) or focal segmental glomerulosclerosis (FSGS)

What does the study involve?
Participants will be randomised to receive either three doses of rituximab infusion or placebo along with standard of care treatment for their disease. Participants are only eligible for the study if they are experiencing a relapse of their disease. If they are randomised to the placebo arm and subsequently relapse again while in the trial, they may be eligible to receive open-label rituximab infusions (identical to the study assessments within the main study.

What are the possible benefits and risks of participating?
Participants have the benefit of accessing rituximab, which is currently not licensed or funded by NHS England for use in adults with relapsing nephrotic syndrome.

Where is the study run from?
Cambridge Clinical Trials Unit based at Cambridge University Hospitals NHS Foundation Trust

When is the study starting and how long is it expected to run for?
November 2019 to April 2026

Who is funding the study?
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC), UK

Who is the main contact?
Wisdom Mbama, wisdom.mbama1@nhs.net

Contact information

Type(s)
Scientific

Contact name
Dr Wisdom Mbama

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Additional identifiers

Clinical Trials Information System (CTIS)
2018-004611-50

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
41605

Study information

Scientific Title
A randomised, two-arm (1:1 ratio), double blind, placebo-controlled Phase III trial to assess the efficacy, safety, cost and cost-effectiveness of rituximab in treating de novo or relapsing NS in patients with MCD/FSGS (TURING)

Acronym
TURING

Study objectives
Rituximab prolongs remission of nephrotic syndrome secondary to minimal change disease and focal segmental glomerular sclerosis

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 14/06/2019, London - City & East Research Ethics Committee (Bristol Research Ethics Committee Centre, Whitefriars, Level 3, Block B, Lewins Mead, Bristol, BS1 2NT; +44(0)207 104 8171; nrescommittee.london-cityandeast@nhs.net)

Study design
Randomized; Interventional; Design type: Treatment, Drug

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Nephrotic syndrome, caused by minimal change disease (MCD) and focal segmental glomerulosclerosis (FSGS)

Interventions
112 patients with new presentation or relapsing MCD/FSGS will be recruited. They will be randomised to receive rituximab (2 x 1 g starting within 4 weeks of the start of protocolised prednisolone regimen (Day 0), followed by 1 g at 26 weeks) or placebo (two doses starting within 4 weeks of the start of protocolised prednisolone treatment followed by last done at 26 weeks).
All patients will receive standard of care treatment with prednisolone, with a protocolised dosing regimen. All trial visits will align with standard of care clinic visits wherever possible. There are approximately 15 visits (based on 24-month participation in the trial), of which approximately 12 will coincide with standard of care visits for this patient population. The infusion visits of which there are 3 in the main study and then an additional 3 in the open label phase are in addition to standard of care and travel and refreshments will be covered for these. Participants will have blood and urine tests at the hospitals as standard and the results will be be shared as part of the study. Participants will be required to provide four 24-hour urine collection samples to detect proteinuria. Once they have achieved remission, they will also be required to carry out weekly urine protein dipstick testing. Kits will be provided by the sites and instructions will be provided via PIS and Urine dipstick test diaries. The advantage of this frequency of testing is that participants will be aware of a potential relapse sooner than if they were not doing this
testing and will be able to get medical treatment quickly.
Data collection will include proteinuria (protein in urine), serum albumin, renal function and quality of life. The primary endpoint will be the time from partial remission to relapse. Follow-up will continue until all patients have completed at least 24 months of follow-up or have relapsed.

An open-label phase (OLP) will be open to patients in the placebo arm who reach the primary endpoint of relapse during the 2-year follow-up visits. Sites will be unblinded to treatment identities per patient at this point and if the relapsed patient is found to be on the placebo arm; they will be offered rituximab therapy which will follow the protocolised pathway as per the main study (3 doses in total over 26 weeks). Participants who qualify for OLP will only be required to attend hospital for infusions and AE checks. Travel and refreshment costs will be covered. Blood and urine test as standard will be extracted directly from online renal registries and participants will have consented to this.
Patients who relapse but are found to have been randomised to the rituximab arm will be reverted to standard of care pathways for their disease.
Patients who have not responded to treatment by achieving partial or complete remission at the week 16 visit will leave the trial and return to standard of care treatment. These patients will not receive the third dose of rituximab or placebo at week 26 as they have not demonstrated steroid responsiveness, and ongoing treatment with prednisolone with or without rituximab is likely to be futile.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Rituximab

Primary outcome(s)
Time from partial or complete remission (whichever documented first) to relapse of nephrotic syndrome (assessed via blood and urine test to confirm relapse)

Key secondary outcome(s))
An evaluation of the effect of rituximab on:
1. Proportion of patients achieving partial or complete remission
2. Time to partial or complete remission from Day 0 (SPPR)
3. Serious adverse events (AEs)
4. AE of Special Interest, including infection and steroid-associated side effects
5. Change in urinary PCR/24 hour proteinuria
6. Change in serum albumin
7. Kidney function as assessed by the change in Glomerular filtration rate (GFR) from Day 0 - Start of Protocolised Prednisolone Regimen (SPPR) to 24 months and to trial end
8. Health Status (EQ-5D-5L)
9. Resource use, cost and cost-effectiveness

Completion date
30/04/2026

Eligibility

Key inclusion criteria
1. Age 16 years or older
2. NS at trial entry (serum albumin <35 g/l and protein creatinine ratio (PCR) >300 mg/mmol) secondary to MCD/FSGS with

3. De novo disease or relapsing disease in a patient previously steroid or calcineurin inhibitor (CNI) responsive
4. Latest biopsy (at any time) proven MCD/FSGS
5. Ability to provide written informed consent
6. Agreed to be enrolled in the National Registry of Rare Kidney Disease (RaDaR)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
16 years

Upper age limit
100 years

Sex
All

Total final enrolment
150

Key exclusion criteria
1. MCD or FSGS due to secondary causes, including obesity-driven hyperfiltration, remnant kidneys, malignancy of a type likely to be associated with MCD /FSGS and genetic polymorphisms known to be associated with nephrosis
2. MCD/FSGS secondary to malignancy, including lymphoproliferative disorders
3. Family history of MCD or FSGS in a first degree relative
4. Previous rituximab within 18 months preceding Day 0 (SPPR), or 12 months if there is evidence of B cell return in peripheral lymphocyte subsets
5. Previous cyclophosphamide within 6 months preceding Day 0 (SPPR)
6. Prednisolone daily dose equal to or greater than 60mg, with a course length of greater than4 weeks, immediately prior to randomisation
7. Evidence of current or past infection with Hepatitis B, C or HIV (unless appropriate prophylaxis is given and no replicating virus is detected)
8. Positive serum pregnancy test (within 14 days prior to treatment with IMP in main trial and rituximab in OLP)
9. Evidence of active severe infection
10. Severe heart failure or severe, uncontrolled cardiac disease
11. Pregnant or breast-feeding women
12. Live vaccine administration in the four weeks prior to enrolment and while remaining on IMP treatment
13. Previous/known hypersensitivity to prednisolone or IMP or to murine proteins (and any excipients as described in section 6.1 of the SmPC)
14. Co-enrolment in another clinical trial of an investigational medicinal product
15. Any other reason which, in the opinion of the Principal Investigator (PI), renders the patient

unsuitable for the trial
16. An increase in CNI dose in the four weeks preceding randomisation

Date of first enrolment
01/07/2019

Date of final enrolment
31/03/2024

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Study participating centre
Addenbrookes Hospital
Cambridge University Hospitals NHS Foundation Trust
Hills Road
Cambridge
England
CB2 0QQ

Study participating centre
St Mary's Hospital
Imperial College Healthcare NHS Trust
Praed Street
London
England
W2 1NY

Study participating centre
Royal Free Hospital
Royal Free London Nhs Foundation Trust
Pond Street
London
England
NW3 2QG

Study participating centre
The Royal London Hospital
Barts Health NHS Trust
Whitechapel
Greater London
London
England
E1 1BB

Study participating centre
John Radcliffe Hospital
Oxford University Hospitals NHS Foundation Trust
Headley Way
Headington
Oxford
England
OX3 9DU

Study participating centre
King's College Hospital NHS Foundation Trust
Denmark Hill
London
England
SE5 9RS

Study participating centre
Royal Derby Hospital
University Hospitals Of Derby And Burton NHS Foundation Trust
Uttoxeter Road
Derby
England
DE22 3NE

Study participating centre
Royal Stoke University Hospital
University Hospitals Of North Midlands NHS Trust
Newcastle Road
Stoke-on-trent
England
ST4 6QG

Study participating centre
St George's Hospital
St George's University Hospitals NHS Foundation Trust
Blackshaw Road
Tooting
London
England
SW17 0QT

Study participating centre
Leicester Royal Infirmary
Infirmary Square
Leicester
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LE1 5WW

Study participating centre
Royal Preston Hospital
Sharoe Green Lane
Fulwood
Preston
England
PR2 9HT

Study participating centre
Manchester University NHS Foundation Trust
Cobbett House
Oxford Road
Manchester
England
M13 9WL

Study participating centre
Guy's Hospital
Guy's & St Thomas' NHS Foundation Trust
Great Maze Pond
London
England
SE1 9RT

Study participating centre

Royal Liverpool University Hospital
Royal Liverpool and Broadgreen University Hospitals NHS Trust
Prescot Street
Liverpool
England
L7 8XP

Study participating centre
York Hospital
York Teaching Hospital NHS Foundation Trust
Wigginton Road
York
England
YO31 8HE

Study participating centre
Southmead Hospital
North Bristol NHS Trust
Southmead Road
Westbury-on-Trym
Bristol
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BS10 5NB

Study participating centre
Royal Sussex County Hospital
Eastern Road
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BN2 5BE

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Broomfield Hospital
Court Road
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CM1 7ET

Study participating centre
St Helier Hospital
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Study participating centre
Queen Elizabeth Medical Centre
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B15 2TH

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NG7 2UH

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Freeman Hospital
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High Heaton
Newcastle-upon-tyne
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NE7 7DN

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Lister Hospital
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SG1 4AB

Study participating centre
Royal Berkshire Hospital
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Study participating centre
Hull Royal Infirmary
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S5 7AU

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Barrack Road
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EX2 5DW

Study participating centre
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Clifford Bridge Road
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CV2 2DX

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Derriford Hospital
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Study participating centre
Salford Royal
Stott Lane

Salford
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M6 8HD

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Beckett Street
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LS9 7TF

Study participating centre
Birmingham Women's And Children's NHS Foundation Trust
Steelhouse Lane
Birmingham
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B4 6NH

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1055 Great Western Road
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Study participating centre
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CF14 4XW

Study participating centre
NHS Ayrshire and Arran
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Boswell House
10 Arthur Street
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KA7 1QJ

Study participating centre
Queen Elizabeth Hospital
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PE30 4ET

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: 17/83/06

Results and Publications

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 database will be hosted by the University of Cambridge server and access will be restricted to delegated individuals only.

IPD sharing plan summary
Stored in non-publicly available repository