

# The use of rituximab in the treatment of nephrotic glomerulonephritis (TURING)

<b>Submission date</b> 17/06/2019	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 21/06/2019	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 07/05/2025	<b>Condition category</b> Urological and Genital Diseases	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> 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effective in most of the patients, recurrent relapses happen in 75% of the patients when the steroid dose is reduced or withdrawn.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?

1. Katrina Gatley (scientific), [katrina.gatley1@nhs.net](mailto:katrina.gatley1@nhs.net)

2. Wisdom Mbama, [wisdom.mbama1@nhs.net](mailto:wisdom.mbama1@nhs.net)

## Contact information

### Type(s)

Scientific

### Contact name

Dr Katrina Gatley

### Contact details

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### Type(s)

Public

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# Additional identifiers

## EudraCT/CTIS number

2018-004611-50

## IRAS number

## ClinicalTrials.gov number

Nil known

## Secondary identifying numbers

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

## 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 patient information sheet

## **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 dose 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 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 measure**

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

**Secondary outcome measures**

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

**Overall study start date**

01/11/2018

**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

**Age group**

Adult

**Lower age limit**

16 Years

**Sex**

Both

### **Target number of participants**

Planned Sample Size: 112; UK Sample Size: 112

### **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 than 4 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**

England

Scotland

United Kingdom

Wales

**Study participating centre**

**Addenbrookes Hospital**

Cambridge University Hospitals NHS Foundation Trust  
Hills Road  
Cambridge  
United Kingdom  
CB2 0QQ

**Study participating centre**

**St Mary's Hospital**

Imperial College Healthcare NHS Trust  
Praed Street  
London  
United Kingdom  
W2 1NY

**Study participating centre**

**Royal Free Hospital**

Royal Free London Nhs Foundation Trust  
Pond Street  
London  
United Kingdom  
NW3 2QG

**Study participating centre**

**The Royal London Hospital**

Barts Health NHS Trust  
Whitechapel  
Greater London  
London  
United Kingdom  
E1 1BB

**Study participating centre**

**John Radcliffe Hospital**

Oxford University Hospitals NHS Foundation Trust  
Headley Way  
Headington  
Oxford  
United Kingdom  
OX3 9DU

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

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

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

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

**Study participating centre**  
**Leicester Royal Infirmary**  
Infirmary Square  
Leicester  
United Kingdom  
LE1 5WW



**Study participating centre**

**Royal Preston Hospital**

Sharoe Green Lane  
Fulwood  
Preston  
United Kingdom  
PR2 9HT

**Study participating centre**

**Manchester University NHS Foundation Trust**

Cobbett House  
Oxford Road  
Manchester  
United Kingdom  
M13 9WL

**Study participating centre**

**Guy's Hospital**

Guy's & St Thomas' NHS Foundation Trust  
Great Maze Pond  
London  
United Kingdom  
SE1 9RT

**Study participating centre**

**Royal Liverpool University Hospital**

Royal Liverpool and Broadgreen University Hospitals NHS Trust  
Prescot Street  
Liverpool  
United Kingdom  
L7 8XP

**Study participating centre**

**York Hospital**

York Teaching Hospital NHS Foundation Trust  
Wigginton Road  
York  
United Kingdom  
YO31 8HE

**Study participating centre**

**Southmead Hospital**

North Bristol NHS Trust  
Southmead Road  
Westbury-on-Trym  
Bristol  
United Kingdom  
BS10 5NB

**Study participating centre**

**Royal Sussex County Hospital**

Eastern Road  
Brighton  
United Kingdom  
BN2 5BE

**Study participating centre**

**Broomfield Hospital**

Court Road  
Chelmsford  
United Kingdom  
CM1 7ET

**Study participating centre**

**St Helier Hospital**

Wrythe Lane  
Carshalton  
United Kingdom  
SM5 1AA

**Study participating centre**

**Queen Elizabeth Medical Centre**

Edgbaston  
Birmingham  
United Kingdom  
B15 2TH

**Study participating centre**

**Queens Medical Centre**

Derby Road  
Nottingham

United Kingdom  
NG7 2UH

**Study participating centre**

**Freeman Hospital**

Freeman Road  
High Heaton  
Newcastle-upon-tyne  
United Kingdom  
NE7 7DN

**Study participating centre**

**Lister Hospital**

Coreys Mill Lane  
Stevenage  
United Kingdom  
SG1 4AB

**Study participating centre**

**Royal Berkshire Hospital**

London Road  
Reading  
United Kingdom  
RG1 5AN

**Study participating centre**

**Hull Royal Infirmary**

Anlaby Road  
Hull  
United Kingdom  
HU3 2JZ

**Study participating centre**

**Northern General Hospital**

Herries Road  
Sheffield  
United Kingdom  
S5 7AU

**Study participating centre**  
**Royal Devon & Exeter Hospital**  
Barrack Road  
Exeter  
United Kingdom  
EX2 5DW

**Study participating centre**  
**Walsgrave General Hospital**  
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Coventry  
United Kingdom  
CV2 2DX

**Study participating centre**  
**Derriford Hospital**  
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PL6 8DH

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**Salford Royal**  
Stott Lane  
Salford  
United Kingdom  
M6 8HD

**Study participating centre**  
**St. James's University Hospital**  
Beckett Street  
Leeds  
United Kingdom  
LS9 7TF

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

**Study participating centre**  
**Gartnavel Royal Hospital**  
1055 Great Western Road  
Glasgow  
United Kingdom  
G12 0XH

**Study participating centre**  
**Cardiff & Vale University LHB**  
Heath Park  
Cardiff  
United Kingdom  
CF14 4XW

**Study participating centre**  
**NHS Ayrshire and Arran**  
PO Box 13  
Boswell House  
10 Arthur Street  
Ayr  
United Kingdom  
KA7 1QJ

**Study participating centre**  
**Queen Elizabeth Hospital**  
Gayton Road  
Kings Lynn  
United Kingdom  
PE30 4ET

## **Sponsor information**

**Organisation**  
Cambridge University Hospitals NHS Foundation Trust

**Sponsor details**  
Addenbrookes Hospital  
Hills Road  
Cambridge

England  
United Kingdom  
CB2 0QQ  
-  
abc@email.com

**Sponsor type**

Hospital/treatment centre

**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**

**Publication and dissemination plan**

Planned publication in a high-impact peer-reviewed journal

**Intention to publish date**

30/12/2027

**Individual participant data (IPD) sharing plan**

The datasets generated during and/or analysed during the current study will be stored in a non-publicly 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