# **Rescue of ADdiSons disease 2**

Submission date 26/09/2012	<b>Recruitment status</b> No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 23/10/2012	<b>Overall study status</b> Completed	<ul> <li>[] Statistical analysis plan</li> <li>[X] Results</li> </ul>
Last Edited 05/01/2021	<b>Condition category</b> Nutritional, Metabolic, Endocrine	Individual participant data

# Plain English summary of protocol

Background and study aims:

Addisons disease is caused by an autoimmune attack leading to destruction of the adrenal glands. RADS2 aims to prevent the autoimmune attack on the adrenal gland and stimulate regrowth and regeneration of adrenal function.

Who can participate?

Patients aged 10 to 65 years, diagnosed with autoimmune Addisons disease within the previous 28 days.

What does the study involve?

Two infusions of rituximab are given, each lasting 6 hours. Also, alternate day injections of an adrenal gland stimulating hormone, ACTH are given.

What are the possible benefits and risks of participating? The benefit is that your adrenal failure might go into remission, or even be cured. The risk is that the trial medication wont work, or that you could have a reaction to it.

Where is the study run from?

Newcastle University, UK, with participating centres in Cambridge and Exeter, UK.

When is study starting and how long is it expected to run for? November 2012, running for 4 years.

Who is funding the study? Medical Research Council, UK.

Who is the main contact? Prof Simon Pearce s.h.s.pearce@ncl.ac.uk

# **Contact information**

**Type(s)** Scientific **Contact name** Prof Simon Pearce

**Contact details** Institute of Genetic Medicine Newcastle University International Centre for Life Newcastle upon Tyne United Kingdom NE1 3BZ +44 (0)191 2418674 s.h.s.pearce@ncl.ac.uk

# Additional identifiers

EudraCT/CTIS number

**IRAS number** 

ClinicalTrials.gov number

Secondary identifying numbers RADS2v2.1:08/12

# Study information

### Scientific Title

Combined immunotherapy and trophic adrenocortical stimulation in new onset autoimmune Addisons disease

### Acronym

RADS2

### **Study objectives**

This study will answer the following principal questions:

In people with new-onset autoimmune Addisons disease, who have residual steroidogenic capacity:

1. Will the therapeutic regimen of rituximab and adrenocorticotropic hormone (ACTH) allow improvement or recovery of adrenocortical function?

2. Will this therapeutic regimen result in amelioration of the humoral immune response by reducing autoantibody titres?

3. What are the adverse effects of this therapeutic regimen?

4. Will the regimen be acceptable and well-tolerated by patients?

5. What is the early natural history of conventionally treated autoimmune Addisons disease (AAD)?

# Ethics approval required

Old ethics approval format

### Ethics approval(s)

National Research Ethics Service (NRES) Committee North East - Sunderland, 24 September 2012, ref: 12/NE/0339

#### Study design

Multicentre study conducted in 2 parts Part A: Open-label interventional study of rituximab and synacthen Part B: Observational study of the natural history of autoimmune Addisons disease

Primary study design

Interventional

**Secondary study design** Non randomised controlled trial

Study setting(s) Hospital

**Study type(s)** Treatment

#### Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

### Health condition(s) or problem(s) studied

Autoimmune Addison's disease

#### Interventions

Part A

1. Subjects will receive 125mg IV methylprednisolone followed by 1g IV rituximab on day 1 & day 15.

2. Depot synacthen 1mg will be self-administered on alternate days (week 1-12, followed by an 8 week tail)

3. Daily oral hydrocortisone and fludrocortisone will continue in regular replacement doses (eg. Hydrocortisone 10 & 5mg, or 10 & 5 & 5mg; fludrocortisone 50-150 ìg)

4. Adrenal function, circulating B cell numbers, adrenal autoantibody titres and wellbeing will be assessed at baseline, 6, 12, 24, 48, and 72 weeks.

5. Replacement steroids will be weaned off, if serum cortisol concentrations improve to >400nmol/l.

The last (72 week) visit of the last participant will mark the end of the study

Part B: Observation only

1. Adrenal function, adrenal autoantibodies and wellbeing will be assessed at baseline & 48 weeks.

2. The last (48 week) visit of the last participant will mark the end of the study for these participants.

### Intervention Type

Other

### Phase

Not Applicable

#### Primary outcome measure

Restoration of normal glucocorticoid secretion (peak cortisol >550nmol/l after repeat synacthen testing at 48 weeks)

### Secondary outcome measures

 Restoration of normal glucocorticoid secretion (peak cortisol >550nmol/l after repeat synacthen testing at 6,12, 24, and 72 weeks)
 Improvement of basal and peak cortisol response (>100nmol/l over baseline) to synacthen testing
 Normalisation of ACTH, Dehydroepiandrosterone (DHEAS), 17á OH-progesterone and recumbent renin and aldosterone levels

# Overall study start date

01/11/2012

# **Completion date**

31/10/2016

# Eligibility

# Key inclusion criteria

Part A:

1. Clear evidence of adrenocortical failure with subnormal cortisol response to 250 μg IV synacthen (peak cortisol <300nmol/l) plus either clinical or biochemical evidence to confirm elevated ACTH, or evidence of mineralcorticoid insufficiency

- 2. Basal or ACTH stimulated serum cortisol >50nmol/l
- 3. Patients are less than 4 weeks from first diagnosis of AAD
- 4. Positive serum 21-hydroxylase autoantibodies (>1.0 IU/l on RSR assay)
- 5. Normal or atrophic adrenal glands on CT scan
- 6. Willingness to travel to the Wilson Horne Immunotherapy Centre, Newcastle for study

7. Willingness to attend education sessions about indications for parenteral glucocorticoid administration and technique of administration

8. Willingness to use secure contraception during and for 12 months post-treatment with rituximab ((women of childbearing potential)

For Part B, only the first 4 criteria are relevant

**Participant type(s)** Patient

Age group

Adult

**Sex** Both

Target number of participants

Part A (15 participants); part B (15 participants)

Total final enrolment

13

### Key exclusion criteria

1. Active viral illness, including HIV, Hepatitis B or C, shingles/Zoster

2. Recent or partially treated TB or unexplained radiographic abnormality on chest X-ray

3 .Previous use of immunosuppressive or cytotoxic drugs (excluding glucocorticoid)

4. Significant cardio-respiratory (inc. asthma), chronic renal or non-autoimmune liver disease

5. Pregnant or breastfeeding and with plan for pregnancy/ breastfeeding within 24 months 6. Known allergy or contraindication to synacthen, synacthen depot, rituximab or methylprednisolone

Date of first enrolment 01/11/2012

# Date of final enrolment

31/10/2016

# Locations

#### **Countries of recruitment** England

United Kingdom

#### **Study participating centre Institute of Genetic Medicine** Newcastle upon Tyne United Kingdom NE1 3BZ

# Sponsor information

# **Organisation** Newcastle upon Tyne Hospitals NHS Foundation Trust

# Sponsor details

Royal Victoria Infirmary Queen Victoria Road Newcastle upon Tyne England United Kingdom NE1 4LP amanda.tortice@ncl.ac.uk

**Sponsor type** Hospital/treatment centre

Website http://www.newcastle-hospitals.org.uk/

ROR https://ror.org/05p40t847

# Funder(s)

**Funder type** Research council

**Funder Name** Medical Research Council (MRC) (UK) ref: MR/J002526

Alternative Name(s) Medical Research Council (United Kingdom), UK Medical Research Council, MRC

**Funding Body Type** Government organisation

Funding Body Subtype National government

**Location** United Kingdom

# **Results and Publications**

**Publication and dissemination plan** Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

**IPD sharing plan summary** Not provided at time of registration

# Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<u>Results article</u>	results	01/04/2020	30/10/2020	Yes	No
Results article	results	01/04/2020	05/01/2021	Yes	No
HRA research summary			28/06/2023	No	No