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Rescue of ADdiSons disease 2

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

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 re-growth 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
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Protocol serial number
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

Primary study design
Interventional

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

Study type(s)
Treatment

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

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

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

Healthy volunteers allowed
No

Age group
Adult

Sex
All

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
United Kingdom

England

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

Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust

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, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

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?
Results article	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