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Regulatory T cells in Type 1 diabetes patients treated with IL-2

Submission date	Recruitment status	[_] Prospectively registered
26/03/2013	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
26/03/2013	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
13/10/2016	Nutritional, Metabolic, Endocrine	

Plain English summary of protocol

Background and study aims
In people with Type 1 diabetes, the bodys immune system, which normally protects against infection and illness, turns around and attacks the cells of the pancreas that produce insulin. Ultimately these cells are destroyed or damaged to a point where they can no longer produce insulin. Researchers in this trial are using a drug called aldesleukin (interleukin-2) at low doses, to see if it can halt this destructive process and rebalance the immune system in people who have recently been diagnosed with Type 1 diabetes, and if so, to determine the appropriate dose needed to do so.

Who can participate?
Participants should be aged 18-50 years and have been diagnosed with Type 1 diabetes within the last two years. People with a previous medical history of organ failure, organ transplant or severe heart disease are not eligible to take part.

What does the study involve?
The study will involve a total of 12 appointments spread over about two months. Most of the visits will take place at Addenbrookes Hospital in Cambridge. During the first visit participants will provide consent and then will be screened to ensure that they are eligible to take part in the study. This will involve a series of tests including a physical exam, a chest x-ray, an electrocardiogram (a test that checks for problems with the electrical activity of your heart) and blood and urine tests. The second visit will involve further tests and then participants will receive aldesleukin (interleukin-2) as an injection just beneath the skin. To minimise the likelihood of side effects from the treatment, very low doses (about 50% less than that previously given to patients) will be used. Over the next nine weeks participants will be asked to attend 10 follow-up visits (five in the first week, two in the second week, and one each in weeks 3, 4 and 9). Each will involve further tests to monitor the participants health. During the study each participant will give a total of 400 ml of blood (less than the amount taken when donating blood).

What are the possible benefits and risks of participating?
There is no guarantee that participants in this study will benefit from taking part. The study medication may halt the destruction of insulin-producing cells in the pancreas for a short while,

but the overall purpose of the study is to see whether aldesleukin (interleukin-2) could be used to benefit people with Type 1 diabetes in future by helping to protect the pancreas from damage. As with all medicines, there is a risk that participants may experience some unwanted side effects. The most common side effects reported as a result of low doses of aldesleukin are flu-like symptoms (fever, shivering, tiredness, runny nose, muscle pain and headaches), temporary soreness or redness at the point where the drug is injected and stomach upset with feelings of nausea, vomiting, abdominal pain or diarrhoea. If participants do experience these side effects, they are only likely to last a short time and will completely clear up afterwards.

Where is the study run from?
University of Cambridge and Cambridge University Hospitals Trust (UK)

When is the study starting and how long is it expected to run for?
The study started in March 2013 and ran until May 2014

Who is funding the study?
Wellcome Trust, JDRF & NIHR Cambridge Biomedical Research Centre (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT01827735

Protocol serial number

13846

Study information

Scientific Title
ADaptive study of IL-2 dose on regulatory T cells in Type 1 Diabetes (DILT1D)

Acronym
DILT1D

Study objectives
Type 1 diabetes is the most common severe chronic autoimmune disease worldwide and is caused by the autoimmune (loss of self tolerance) mediated destruction of the insulin producing pancreatic beta cells thus leading to insulin deficiency and development of hyperglycaemia. Currently, medical management of type 1 diabetes focuses on intensive insulin replacement therapy to limit complications (retinopathy, nephropathy, neuropathy); nevertheless clinical outcomes remain sub optimal. There are intensive efforts to design novel immunotherapies that can arrest the autoimmune process and thereby preserve residual insulin production leading to fewer complications and better clinical outcomes.
The vast majority of genes that contribute to susceptibility to type 1 diabetes have been found to encode proteins involved in immune regulation and function. In particular, several susceptibility proteins are involved in the interleukin 2 (IL-2) pathway that regulates T cell activation and tolerance to self antigens. Aldesleukin (Proleukin) is a human recombinant IL-2 product produced by recombinant DNA technology using genetically engineered E. coli stain containing an analogue of the human interleukin-2 gene. There is substantial nonclinical, preclinical and clinical data that ultra low dose IL-2 (aldesleukin) therapy can arrest the autoimmune mediated destruction of pancreatic beta cells by induction of functional T regulatory cells. However, prior to embarking on large proof of concept trials in type 1 diabetes it is essential that the optimum dose of IL-2 is determined. The objective of this study is to establish in patients with type 1 diabetes the optimal dose of IL-2 to administer in order to increase T regulatory cell response.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Cambridge Central REC, First MREC approval date 18/02/2013, ref: 13/EE/0020

Primary study design
Interventional

Study design
Non-randomised; Interventional; Design type: Treatment

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: Diabetes Research Network; Diabetes Type 1

Interventions
Drug: Aldesleukin (Proleukin)
A single, subcutaneous dose will be administered with the maximum dose allowed 1.5 X 106 IU /M2.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome(s)
T regulatory cell response; Timepoint(s): The maximum value observed in each patient's profile over the first 7 days of the follow up period.

Key secondary outcome(s)
No secondary outcome measures

Completion date
15/05/2014

Eligibility

Key inclusion criteria
Current inclusion criteria as of 23/08/2013:
1. Type 1 diabetes
2. 18-50 years of age
3. Duration of diabetes less than 24 months from diagnosis
4. One positive auto-antibody (anti-islet cell, anti-GAD, anti-IA2, anti-ZnT8)

Previous inclusion criteria:
1. Type 1 diabetes
2. 18-50 years of age
3. Duration of diabetes more than 3 months but less than 24 months from diagnosis
4. One positive auto-antibody (anti-islet cell, anti-GAD, anti-IA2, anti-ZnT8)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
50 Years

Sex
All

Key exclusion criteria
Current exclusion criteria as of 23/08/2013:
1. Hypersensitivity to aldesleukin or any of the excipients
2. History of severe cardiac disease
3. History of malignancy within the past 5 years (with the exception of localized carcinoma of the skin that had been resected for cure or cervical carcinoma in situ
4. History or concurrent use of immunosuppressive agents or steroids.
5. History of unstable diabetes with recurrent hypoglycaemia
6. Active autoimmune, hyper or hypothyroidism
7. Active clinical infection
8. Major pre-existing organ dysfunction
9. Previous organ allograft
10. Females who are pregnant, lactating or intend to get pregnant during the study
11. Male who intend to father a pregnancy during the study
12. Donation of more than 500 ml of blood within 2 months prior to aldesleukin administration
13. Participation in a previous therapeutic clinical trial within 2 months prior to aldesleukin administration
14. Abnormal ECG
15. Abnormal full blood count, chronic renal failure, and/or impaired liver function
16. Positive HBsAg or HepC serology or HIV test
17. Any medical history or clinically relevant abnormality that is deemed by the principal investigator and/or medical monitor to make the patient ineligible for inclusion because of a safety concern

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Date of first enrolment
01/03/2013

Date of final enrolment
15/05/2014

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Cambridge Institute for Medical Research
Cambridge
United Kingdom
CB2 0XY

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation trust & University of Cambridge (UK)

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Government

Funder Name
Juvenile Diabetes Research Foundation

Alternative Name(s)
Juvenile Diabetes Research Foundation Ltd, JUVENILE DIABETES RESEARCH FOUNDATION LIMITED, JDRF UK, JDRF

Funding Body Type
Government organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Funder Name
National Institute for Health Research - Cambridge Biomedical Research Centre

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Wellcome Trust (UK) Grant Codes: 091157/Z/10/Z

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

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	11/10/2016		Yes	No
Protocol article	protocol	04/06/2014		Yes	No
HRA research summary			28/06/2023	No	No
Other publications	recruitment analysis	11/03/2015		Yes	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes