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Phase 1b study of proinsulin (PI) peptide immunotherapy in new onset type 1 diabetes

Submission date
06/06/2011

Recruitment status
No longer recruiting

Registration date
28/07/2011

Overall study status
Completed

Last Edited
08/01/2020

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Type 1 diabetes (insulin-dependent diabetes) is caused by the body's own white blood cells damaging the insulin producing cells in the pancreas. Our aim is to develop a treatment that can slow or stop this process by switching off the white blood cells causing the damage. At present we are at quite an early stage in this research. In a previous study we were able to show in people who had had diabetes a long time that giving 3 injections of a small part of one of the molecules in the beta cells, proinsulin, appeared safe and may begin to switch off the white blood cells that are causing the damage. In this study, we are looking to see if this is also true in people who have newly-diagnosed diabetes. We will also be testing whether giving more than three injections is more effective, and whether this treatment can slow or stop the loss of insulin from the pancreas in the year after people are diagnosed.

Who can participate?
To take part you need to be aged 18-40, diagnosed with type 1 diabetes and have received your first insulin injection within 100 days of entering the trial.

What does the study involve?
If you take part, first of all, you will be asked to give a small sample of blood to test your tissue type and the antibodies to the pancreas in your blood. This sample will be taken in the same way as any standard blood test. Only around one half of people with type 1 diabetes have the right tissue type to respond to the particular fragment of proinsulin we are testing. If the first test shows you have antibodies to the pancreas and the right tissue type for the study, you will be asked to come to your local research centre for a general examination and further blood tests including a test of the amount of insulin your body still makes in the 2 hours after a standard liquid meal. If you still have some insulin response after the meal (80-90% of people do within the first year after diagnosis) you will be contacted by the research team to arrange the first injection treatment of the study. The treatments involve a very tiny, almost painless injection under the skin of the arm given in a very similar way to vaccination injections. Everyone in the trial will receive injections every 2 weeks for 24 weeks and then check-ups for another 24 weeks. People in the trial will be in one of three groups. Group A will receive only salt water injections (placebo). Group B will receive peptide injections every 4 weeks with saline injections in between. Group C will receive peptide injections every 2 weeks. Neither you nor the person

giving you the injections will know until the end of the study which group you are in and which injections you are receiving. Also no one can chose which group you go into: this is done randomly by a computer programme so that everyone has an equal chance of being in any particular group. During the treatment, you will be asked to provide blood samples to test the response of your body's immune system and to pick up any side effects and on 3 occasions we will do the mixed meal tolerance test again to see how much insulin your body is making. The amounts of blood taken will be larger than usual to allow special laboratory tests to be performed. At the end of this test we will ask you for a urine sample to send to the research lab. You will not be told the results of the tests until the end of the trial unless any of the results are not normal and need treatment. The total blood volume taken from you whilst you are on the trial will be within the guidelines of the National Institute of Health, USA. Every 2 weeks you will be contacted by a nurse or doctor with training in diabetes to discuss your insulin treatment and blood sugar levels and help make sure your insulin treatment is keeping your sugar levels in a good range.

What are the possible benefits and risks of participating?
During the research project your diabetes will be very closely monitored, you will receive regular input from a nurse to help with your diabetes as well as regular check-ups including routine blood testing. If you are in the group that receives the 'active' peptide injection, it is possible that it will help keep your pancreas making insulin for longer but we cannot say this for certain until we have completed this and further research studies. There may be bruising and discomfort at the site of the blood test as with any blood test. The amounts of blood we are taking are small enough that they should not make you feel fatigue or cause anaemia. There may be local red reactions at the site of the injections. It is possible that you might have a severe reaction to the injection requiring treatment. However, we have not seen any severe reactions in the 37 people who have received this injection so far. All injections will be given with trained staff and equipment on hand if you should have any problems. If you do have a severe reaction, no further injections will be given. It is theoretically possible that if you are in the group that receives injections of 'active' peptide that they might weaken the insulin production from your pancreas. This has not been seen in previous studies and we will be testing you for insulin production every 12 weeks.

Where is the study run from?
It is being organised by Cardiff University and King's College London. There are four hospitals participating:
1. University Hospital of Wales, Cardiff
2. Guys Hospital, London
3. Bristol Royal Infirmary, Bristol
4. Royal Victoria Infirmary, Newcastle.

When is the study starting and how long is it expected to run for?
From July 2011 to February 2015.

Who is funding the study?
This study is being funded by the Diabetes Vaccine Development Centre in collaboration with the Juvenile Diabetes Research Foundation International.

Who is the main contact?
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

ClinicalTrials.gov (NCT)
NCT01536431

Protocol serial number
SPON817-10

Study information

Scientific Title
Phase 1b study of proinsulin (PI) peptide immunotherapy in new onset type 1 diabetes

Acronym
MonoPepT1De-1b

Study objectives
The aim of the study is to examine the safety of i.d. administration of the naturally processed proinsulin peptide C19-A3 (PPI C19-A3) at a dose of 10 ìg every 14 days or every 28 days for a total of 12 and 6 doses, respectively, to patients with new-onset Type 1 diabetes
The objectives of this study are:
1. To examine the risk of C19-A3 administration in terms of general safety, induction of hypersensitivity and disease acceleration
2. To examine the effects of C19-A3 administration on appropriate biomarkers of disease (pro-inflammatory autoreactive T lymphocytes) and immune regulation (autoreactive regulatory T cells)
3. To examine any benefits of 14-day as compared to 28-day dosing

On 22/04/2015 the overall trial end date was changed from 31/12/2012 to 16/02/2015.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee South West - Exeter, REC, 25/03/2011, ref: 08/H0206/58

Study design
Multi-centre randomised double-blind placebo-controlled three-arm study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Newly diagnosed type 1 diabetes

Interventions
1. Study drug will be administered intradermally at a frequency of either bi-weekly or 4 times a week
2. To maintain blinding, all subjects will receive injections at bi-weekly intervals
3. In the case of the placebo group this will be normal saline only
4. For the Low Frequency dosing group this will be alternate study drug and normal saline only
5. For the High Frequency dosing group this will be study drug on every occasion
6. Injections will be administered over 22 weeks to achieve a total of 12
7. Thus the cumulative dose in the Low Frequency group will be 60ìg and in the High Frequency group 120 ìg

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Proinsulin peptide C19-A3 (PPI C19-A3)

Primary outcome(s)
Assessment of the safety of PPI C19-A3 peptide administration in subjects with new-onset Type 1 diabetes

Key secondary outcome(s))
1. Change in stimulated C-peptide production at 12, 24, 36 and 48 weeks versus baseline and between groups
2. Change in level or quality of T lymphocyte biomarkers of alpha cell specific immune response at 12, 24, 36 and 48 weeks versus baseline and between groups
3. Change in level or quality of islet cell autoantibody biomarkers of alpha-cell specific immune response at 12, 24, 36 and 48 weeks versus baseline and between groups
4. Change in glycated haemoglobin (as measured by % HbA1c levels), daily insulin usage, and mean amplitude of glucose excursions at 12, 24, 36 and 48 weeks versus baseline and between

groups
5. Changes in the Hypoglycaemia Fear Survey (HFS), and Diabetes Treatment Satisfaction Questionnaire (DTSQs) scores at 3,6 and 12 months and ADDQoL (Audit of Diabetes-Dependent Quality of Life) at 6, and 12 months versus baseline and between groups
6. The DTSQc (Diabetes Treatment Satisfaction Questionnaire, change version) will also be compared between groups at 12 months

Completion date
16/02/2015

Eligibility

Key inclusion criteria
1. Age 18-40 years
2. Diagnosis of Type 1 diabetes within the last 100 days (dated from the first insulin injection)
3. Possession of HLA-DRB1*04:01 allele
4. At least one positive islet cell autoantibody (ie anti-GAD65, antibodies to insulinoma-associated antigen-2 (IA-2) or zinc transporter 8 (ZnT8)).
5. Peak insulin C-peptide >200 pmol/L (at any time point after stimulation with Mixed Meal Tolerance Test)
6. Written and witnessed informed consent to participate

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
40 years

Sex
All

Key exclusion criteria
1. Females who are pregnant, breast-feeding or not using adequate forms of contraception
2. Use of immunosuppressive or immunomodulatory therapies, including systemic steroids within 1 month prior to randomisation and any monoclonal antibody therapy given for any indication
3. Any other medical condition which, in the opinion of investigators, could affect the safety of the subject's participation
4. Recent subject's involvement in other research studies which, in the opinion of investigators,

may adversely affect the safety of the subjects or the results of the study
5. Subjects should not have had immunisations with live or killed vaccines or allergic desensitisation procedures less than 1 month prior to their first treatment

Date of first enrolment
14/02/2012

Date of final enrolment
19/03/2014

Locations

Countries of recruitment
United Kingdom

England

Wales

Study participating centre
University Hospital of Wales
Cardiff
United Kingdom
CF14 4XW

Study participating centre
Guy's Hospital
London
United Kingdom
SE1 9RT

Study participating centre
Bristol Royal Infirmary
Bristol
United Kingdom
BS2 8HW

Study participating centre
Royal Victoria Infirmary
Newcastle
United Kingdom
NE1 4LP

Sponsor information

Organisation
Cardiff University

ROR
https://ror.org/03kk7td41

Organisation
Kings College London

Funder(s)

Funder type
Charity

Funder Name
Juvenile Diabetes Research Foundation (United Kingdom)

Funder Name
Diabetes Vaccine Development Centre (United Kingdom)

Alternative Name(s)
DVDC

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
Australia

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	09/08/2017	22/01/2019	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes