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Enhanced epidermal antigen specific immunotherapy trial - Type 1 Diabetes

Submission date
17/06/2016

Recruitment status
No longer recruiting

Registration date
06/09/2016

Overall study status
Completed

Last Edited
12/08/2022

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Type 1 diabetes is caused by the body's own white blood cells damaging the insulin-producing cells in the pancreas. The pancreas is then unable to produce any insulin, a hormone that normally controls the amount of sugar (glucose) in the blood. This results in the blood glucose level becoming too high. The aim is to develop a treatment that can slow or stop this process by switching off the white blood cells causing the damage. This treatment involves a molecule similar to insulin attached to small particles of gold (nanoparticles). The aim of this study is to investigate whether this treatment is safe with no significant side-effects.

Who can participate?
Patients aged between 18 and 40 with type 1 diabetes

What does the study involve?
Participants have a blood test to assess whether they have the right tissue type for the study. If suitable, they are asked to attend their local research centre for a general examination and further blood and urine tests. If the participant still has some insulin response after the post-meal urine test they are given the first injection. Each participant has three injections of the same treatment, given 4 weeks apart. During the treatment, participants undergo various tests including blood and urine tests and lymph node tissue samples (biopsies). A follow-up appointment takes place 6 weeks after the last injection.

What are the possible benefits and risks of participating?
Participants will have more time with staff members to discuss their diabetes and ask questions than at a routine clinic appointment. It is not known whether receiving the injections will be of benefit, as this is the first study where the treatment is being used in humans. Possible side effects include bruising and discomfort at the site of the blood test and lymph node tests, local redness and swelling reactions at the site of the injections, and severe allergic reaction to the injection requiring treatment, such as steroids, adrenaline or fluids.

Where is the study run from?
1. Cardiff & Vale University Health Board (UK)
2. Linköping University Hospital (Sweden)

When is the study starting and how long is it expected to run for?
August 2016 to January 2020 (updated 12/12/2019, previously: December 2018)

Who is funding the study?
Seventh Framework Programme

Who is the main contact?
1. Prof. Colin Dayan (DayanCM@cardiff.ac.uk)
2. Rachel Stenson (StensonR@cardiff.ac.uk)
(updated 12/12/2019, previously: Julie Pell (pelljc@cardiff.ac.uk))

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Public

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Additional identifiers

EudraCT/CTIS number

2015-003934-28

IRAS number

ClinicalTrials.gov number
NCT02837094

Secondary identifying numbers
SPON1455-15

Study information

Scientific Title
Enhanced Epidermal Antigen Specific Immunotherapy trial -1 (EE-ASI-1): a Phase 1a study of gold nanoparticles administered intradermally by microneedles to deliver immunotherapy with a proinsulin derived peptide in Type 1 diabetes

Acronym
EE-ASI-1

Study objectives
To explore the safety of antigen specific immunotherapy using very small (< 5nm) gold nanoparticles coupled to a peptide of proinsulin C19-A3.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London - City & East Research Ethics Committee, 04/03/2016, ref: 16/LO/0020

Study design
Non-randomised study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied

Type 1 diabetes

Interventions
IMP: C19-A3 GNP (gold nanoparticles) injected by Nanopass microneedles

Participants will have a blood test to assess whether they have the right tissue type for the study. If suitable, they will be asked to attend their local research centre for a general examination and further blood and urine tests. If the participant still has some insulin response after the post meal urine test they will proceed to the first injection. Each participant will have three injections of the same treatment, these are given 4 weeks apart. During the treatment, participants will undergo various monitoring including blood and urine tests, mixed meal tolerance tests, lymph node biopsies. A follow-up appointment will take place 6 weeks after the last injection.

Intervention Type
Drug

Phase
Phase I

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

Primary outcome measure
The safety (adverse event) profile of the investigational agent. The following time points are set for evaluation of adverse event profiles, but pharmacovigilance data will be collected at times points in between if events arise: 2 hours, 4 weeks, 8 weeks and 14 weeks

Secondary outcome measures
1. T cell responses to GNP C19A3 as determined by changes from baseline of interferon gamma and IL10 ELISPOT responses to this peptide in blood following treatment at weeks 0, 8 and 14
2. T cell responses to GNP C19A3 as determined by changes from baseline of interferon gamma and IL10 ELISPOT responses to this peptide in draining axillary lymph node before and after the first and last treatment administration
3. Changes in additional immunological biomarkers (e.g. flow cytometry profiles, T reg assays, beta cell and T-cell cell-free DNA markers) from baseline at week 0, 8 and 14
4. Effects on residual cpeptide secretion at week 12 as compared to baseline as assessed by a mixed meal tolerance
test and a stimulated urine cpeptide test
5. Effects on glycaemic control assessed by blood sugar profiles and HbA1c at week 14 as compared to baseline
6. Questionnaires on quality of life and diabetes self-management at baseline and week 14

Overall study start date
01/08/2016

Completion date
31/12/2019

Eligibility

Key inclusion criteria
1. Clinical diagnosis of type 1 diabetes for > 3 months (dated from the first insulin injection)
2. Commenced on insulin treatment within 1 month of diagnosis
3. Age 16 to 40 years
4. 2 hour post-meal UCPCR > 0.53 nmol/mmol on at least one occasion (maximum 3 tests on different days)
5. Possession of 0401 allele at the HLA-DRB1 gene locus
6. The following birth control methods should be used (considered highly effective with a failure rate of less than 1% per year when used consistently and correctly):
6.1. Combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation:
6.1.1. Oral
6.1.2. Intravaginal
6.1.3. Transdermal
6.2. Progestogen-only hormonal contraception associated with inhibition of ovulation:
6.2.1. Oral
6.2.2. Injectable
6.2.3. Implantable
6.3. Intrauterine device (IUD)
6.4. Intrauterine hormone-releasing system (IUS)
6.5. Bilateral tubal occlusion
6.6. Vasectomised partner (provided that the partner is the sole sexual partner of the trial participant and that medical assessment of azoospermia has been confirmed)
6.7. Sexual abstinence (defined as refraining from heterosexual intercourse during the duration of the trial)
7. Written and witnessed informed consent to participate

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
8

Total final enrolment
6

Key exclusion criteria
1. HbA1c > 86mmol/L (10%)
2. Females who are pregnant, breastfeeding or not using adequate forms of contraception
3. Previous diagnosis of renal disease including glomerulonephritis or nephropathy
4. Raised serum creatinine or abnormal urine albumin/creatinine ratio (ACR) (values above the laboratory reference range). If the initial ACR is raised, this should be repeated on two further occasions as first morning samples. The subject can be included if both of these samples are negative (within the reference range)
5. Use of immunosuppressive or immunomodulatory therapies, including systemic steroids

within 1 month prior to receiving the IMP and any monoclonal antibody therapy given for any indication. Note that previous exposure to proinsulin peptide C19-A3 in a clinical trial is an exclusion criterion
6. Use of cannabis within one month prior to trial entry
7. Use of any hypoglycaemia agents other than insulin, for more than 6 weeks, at any time prior to trial entry
8. Use of inhaled insulin
9. Known alcohol abuse, drug abuse, HIV or hepatitis
10. Allergies to drug components or any excipients
11. Any other medical condition which, in the opinion of investigators, could affect the safety of the subject's participation or outcomes of the study, including immunocompromised states and autoimmune conditions
12. Subjects should not have had immunisations (flu and others) for 1 month prior to trial entry and should not receive any during their time in the trial – see section 5.6
13. 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
14. Abnormal ECG findings

Date of first enrolment
01/08/2016

Date of final enrolment
30/11/2018

Locations

Countries of recruitment
Sweden

United Kingdom

Wales

Study participating centre
Cardiff & Vale University Health Board
University Hospital of Wales
Heath Park
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CF14 4XW

Study participating centre
Linköping University Hopsital
Medical Faculty
Linköping University and Linköping University Hospital

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Sponsor type
University/education

ROR
https://ror.org/03kk7td41

Funder(s)

Funder type
Other

Funder Name
Seventh Framework Programme

Alternative Name(s)
EC Seventh Framework Programme, European Commission Seventh Framework Programme, EU Seventh Framework Programme, European Union Seventh Framework Programme, FP7

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Publication and dissemination plan
It is intended that the results of the study will be reported and disseminated at international conferences and in peer-reviewed scientific journals. Written feedback will also be provided to the study participants.

Intention to publish date
31/12/2020

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be included in the subsequent results publication.

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results				No	No
Results article		27/01/2022	20/06/2022	Yes	No
Protocol file	version 3.2	06/07/2018	12/08/2022	No	No
HRA research summary			28/06/2023	No	No