

Enhanced epidermal antigen specific immunotherapy trial - Type 1 Diabetes

Submission date 17/06/2016	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 06/09/2016	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 12/08/2022	Condition category Nutritional, Metabolic, Endocrine	<input type="checkbox"/> 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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Additional identifiers

ClinicalTrials.gov (NCT)

NCT02837094

Clinical Trials Information System (CTIS)

2015-003934-28

Protocol serial number

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

Study type(s)

Prevention

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(s)

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

Key secondary outcome(s)

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

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

Healthy volunteers allowed

No

Age group

Adult

Sex

All

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

United Kingdom

Wales

Sweden

Study participating centre

Cardiff & Vale University Health Board

University Hospital of Wales

Heath Park

Cardiff

United Kingdom

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Study participating centre

Linköping University Hospital

Medical Faculty

Linköping University and Linköping University Hospital

Linköping

Sweden

SE 58185

Sponsor information

Organisation

Cardiff University (UK)

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

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?
Results article		27/01/2022	20/06/2022	Yes	No
Basic results				No	No
HRA research summary			28/06/2023	No	No
Protocol file	version 3.2	06/07/2018	12/08/2022	No	No