

Islet autoantigen-derived peptides eluted from Human Leucocyte Antigen (HLA) class II molecules as vaccines for the immunotherapy of type 1 diabetes: a safety and proof of concept study in man

Submission date

10/02/2006

Recruitment status

No longer recruiting

Registration date

03/03/2006

Overall study status

Completed

Last Edited

17/05/2011

Condition category

Nutritional, Metabolic, Endocrine

☐ Prospectively registered

☐ Protocol

☐ Statistical analysis plan

☒ Results

☐ Individual participant data

Plain English summary of protocol

Not provided at time of registration

Contact information

Type(s)

Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

PI/1-s

Study information

Scientific Title

Study objectives

Type 1 diabetes mellitus is an autoimmune condition resulting in the destruction of pancreatic beta cells, leading to a failure of insulin production.

Hypotheses:

To determine in man whether intradermal administration of a soluble peptide sequence of proinsulin (C19-A3) identified by microelution from HLA-DR4 molecules and shown to be a disease-related T cell epitope by responses in newly-diagnosed patients with diabetes:

1. Is safe, particularly in terms of hypersensitivity reactions over a wide dose range (10 - 100 micrograms) (safety)
2. Can induce a regulated immune response in man (loss of peptide-specific interferon (IFN) gamma+ T cells, induction of peptide specific interleukin-10+ (IL-10+) T cells (proof of concept)

Ethics approval required

Old ethics approval format

Ethics approval(s)

Central and South Bristol Research Ethics Committee on the 16/12/2005 (ref: 05/Q2006/55).

Study design

Open label, phase 1, dose-escalating safety study with control (no treatment) arm (safety). T cell responses will also be measured (blinded) (proof of concept)

Primary study design

Interventional

Secondary study design

Non randomised controlled trial

Study setting(s)

Not specified

Study type(s)

Treatment

Participant information sheet

Health condition(s) or problem(s) studied

Type 1 diabetes mellitus

Interventions

A peptide corresponding to amino-acid C19-A3 of proinsulin will be administered in increasing doses, 10, 100 and 1000 micrograms intradermally in the upper arm. Subjects will be divided into three equal groups, one group for each dose of peptide. Beginning at 10 micrograms, injections will be given on three occasions one month apart before progressing to the next dose in a new group of subjects.

Intervention Type

Drug

Phase

Phase I

Drug/device/biological/vaccine name(s)

Vaccine proinsulin (C19-A3)

Primary outcome measure

1. Adverse event and side-effect profiles of peptide administration
2. Changes in proinsulin peptide-induced IFN-gamma+ or IL-10 response (ratio of maximal stimulation indices) as detected by Enzyme-Linked Immunosorbent Spot (ELISPOT) three months after the first injection compared to baseline

Secondary outcome measures

1. Change in proinsulin peptide induced IFN-gamma+ or IL-10 response ratio six months after the first injection
2. Changes in IFN-gamma+ or IL-10 response ratio to epitopes of GAD65 and IA-2 eluted from HLA-DR4
3. Changes in IL-2, IL-4+ and IL-5+ T cell responses to the antigen panel
4. Changes in anti-insulin, proinsulin, GAD65 and IA-2 antibody levels versus baseline

Overall study start date

19/12/2005

Completion date

31/12/2007

Eligibility

Key inclusion criteria

1. HLA-DRB1 0401 positive patients
2. Aged 18 - 50 with type 1 diabetes of five or more years duration
3. HbA1c less than 10% and no insulin C-peptide production

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

72

Key exclusion criteria

1. C-peptide response to glucagon stimulation test greater than 2 nmol/l
2. Proliferative or pre-proliferative retinopathy or macula oedema
3. Diabetic nephropathy or other severe diabetic complications
4. Asthma
6. Atopy
7. Documented allergy
8. Use of steroids or immunosuppressive drugs
9. Other autoimmune diseases (except thyroiditis)
10. Women not taking effective contraception

Date of first enrolment

19/12/2005

Date of final enrolment

31/12/2007

Locations

Countries of recruitment

England

United Kingdom

Study participating centre

University of Bristol

Bristol

United Kingdom

BS1 3NY

Sponsor information

Organisation

Diabetes Vaccine Development Centre (Australia)

Sponsor details

School of Population Health
University of Melbourne
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Sponsor type

Research organisation

Funder(s)**Funder type**

University/education

Funder Name

University of Melbourne (Australia) - Diabetes Vaccine Development Centre (protocol no: PI/1-S)

Results and Publications**Publication and dissemination plan**

Not provided at time of registration

Intention to publish date**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	01/02/2009		Yes	No