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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	Recruitment status
10/02/2006	No longer recruiting
Registration date	**Overall study status**
03/03/2006	Completed
Last Edited	**Condition category**
17/05/2011	Nutritional, Metabolic, Endocrine

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] 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

Protocol serial number
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

Study type(s)
Treatment

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(s)
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

Key secondary outcome(s))
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

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

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

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
United Kingdom

England

Study participating centre
University of Bristol
Bristol
United Kingdom
BS1 3NY

Sponsor information

Organisation
Diabetes Vaccine Development Centre (Australia)

Funder(s)

Funder type
University/education

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

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	01/02/2009		Yes	No