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Transplantation of immunoprotected pancreatic islets for the therapy of type 1 diabetes mellitus (T1DM)

Submission date	Recruitment status	[ ] Prospectively registered
18/03/2009	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
30/06/2009	Completed	[X] Results
Last Edited	**Condition category**	[ ] Individual participant data
30/06/2009	Nutritional, Metabolic, Endocrine	

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
19382 PRE805

Study information

Scientific Title

Microencapsulated pancreatic islet allografts into nonimmunosuppressed patients with type 1 diabetes mellitus: a phase I single-arm single-centre pilot trial

Study objectives
Pancreatic islet allografts into patients with type 1 diabetes mellitus (T1DM) are subject to both immune rejection and autoimmune recurrency of disease if the recipients are not adequately and generally immunosuppressed. Unfortunately most of immunosuppressive agents, whether are they of pharmacological or biological nature are associated with severe, attending risk for serious complications, at level of different organs and apparatuses. In order to circumvent need for the recipint's general immunosuppression we had developed since the mid '80s a method to envelop the isolated islets within highly biocompatible and selective permeable microcapsules, based on alginic acid (a polysaccharide extracted from brown seaweeds) and aminoacidic polycations. Such microcapsules, implemented over the years have been extensively employed in pre-clinical trials where either low or high mammal animal models with either induced or spontaneous diabetes underwent graft of microencapsulated islets. The particular nature and composition of the capsules make these artificial shields very suitable for easy injection in the recipients' peritoneal cavity, with no induction, due to their high biocompatibility, of any inflammatory cell response. The positive results obtained in rodents with spontaneous diabetes (nonobese diabetic [NOD] mice) where encapsulated islet xenografts (rat to mouse; pig to mouse; human to mouse) were able to reverse hyperglycemia for extraordinary long periods of time prompted us to scale up to dogs, and recently mokeys with spontaneous or induced diabetes. Also in these higher mammals positive results were obtained in terms of both, correction of hyperglycemia and absence of inflammatory cell overgrowth of the capsules. Having completed the pre-clinicals we turned our attention to humans. In order to make our capsules suitable for human application we have upscaled our system for ultrapurification of the basic capsules' constituent (alginic acid) so as to obtain a pyrogen-free, endotoxin-free alginic acid (according to FDA guidelines) that is low in protein content (<0.4%, according to the 'bioinvisibility' criterion laid out by FDA).

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Italian Ministry of Health, approved on 05/09/2003
2. Ethics Committee of University of Perugia, approved on 15/01/2004

Primary study design
Interventional

Study design
Phase I single-arm single-centre pilot trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Type 1 diabetes mellitus

Interventions
Graft of human pancreatic islet containing microcapsules made of alginic acid and poly-L-ornithine. Upon an overnight insulin feed-back, in order to achieve and sustain normoglycemia,

the patients undergo, under local anesthesia and echography guidance, a samll abdominal incision to allow passage of a 14G polyethylene catheter connected to a 60 ml syringe luer. The capsules (packed tissue volume = 50 ml) upon suspension in sterile saline will be slowly injected (10 min) through the syringe into the patient's peritoneal cavity. Echography monitoring of the process is insured. Upon termination of the procedure the capsules are visualised echographycally.

The trial is taking place at the University of Perugia Hospital and Clinics.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Pancreatic islet allografts

Primary outcome(s)
1. Blood glucose (by reflectometer)hourly the first 7 days, thereafter 4 times a day as per usual clinical protocols for diabetes care
2. Serum C-peptide (radioimmunoassay) hourly the first 7 days, thereafter once a week in basal and 30 min after meal, throughout 2 years
3. Abdominal CT scan (1-6 months)

Key secondary outcome(s)
1. Blood glucose levels. Timepionts: hourly during the first 72 hours post-transplant, thereafter 6 times a day until 2 years post-transplantation (end of protocol)
2. Serum C-peptide. Timepoints: hourly during the first 72 hours and thereafter twice a day until 2 weeks post-transplantation (basal, 60 min after breakfast), thereafter once a day (60 min after breakfast) for 3 months, thereafter once monthly (basal + 60 min after breakfast) for 2 years
3. Depending upon obtained blood glucose control (and insulin/C-peptide output) exogenous insulin may be tapered down until suspension if necessary
4. CT scan of the abdomen every 6 months for 2 years
5. The following will be checked regularly until 2 years post-transplantation in order to assess any eventual favourable impact of the encapsulated islet grafts on secondary complications of T1DM:
5.1. Retinography
5.2. Nerve motor and sensorial conduction velocity
5.3. Microalbuminuria (24 hour urines)

Completion date
01/01/2012

Eligibility

Key inclusion criteria
1. Male patients, age range: 20-50 years
2. Patients with long-standing T1DM (over 15 years)

3. On daily quadruple insulin injection therapy regimen
4. No major complications of the disease (pre-proliferative retinopathy, initial microalbuminuria, macrovascular disease)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Male

Key exclusion criteria
1. Female patients (because the capsules were to be implanted intraperitoneally, with possible adverse effects on ovary's function)
2. Patients with advanced complcations of T1DM
3. Patients with neoplasms whatsoever

Date of first enrolment
01/03/2004

Date of final enrolment
01/01/2012

Locations

Countries of recruitment
Italy

Study participating centre
University of Perugia
Perugia
Italy
06126

Sponsor information

Organisation
University of Perugia (Italy)

ROR

https://ror.org/00x27da85

Funder(s)

Funder type
University/education

Funder Name
University of Perugia (Italy)

Funder Name
Inter-University Consortium for Organ Tranplantation (Italy)

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 for first two cases	01/01/2006		Yes	No