Clinical trial results: *A Monocentric, open-label pilot study to assess the safety and efficacy of minimal islet transplantation in patients with new-onset type 1 diabetes*

Summary

EudraCT number*	2014-004110-28
Trial protocol	DRI-MITO 1/2014
Global end of trial date*	02 NOV 2023

Trial information

Trial identification	
Sponsor protocol code*	DRI-MITO 1/2014
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02505893
WHO universal trial number (UTN)	-

Notes:

Sponsors details*	
Sponsor organization name	IRCCS Ospedale San Raffaele
Sponsor organization address	Via Olgettina, 60, Milano, Italy, 20132
Public contact	IRCCS Ospedale San Raffaele; Medicina Generale Indirizzo Diabetologico Via Olgettina 60, 20132 Milano, Italy Telephone: +39 02 26432961 Email: piemonti.lorenzo@hsr.it
Scientific contact	Lorenzo Piemonti

Notes:

Paediatric regulatory details*	
Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes or No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes or No

Results analysis stage	
Analysis stage*	Final
Date of interim/final analysis*	1 Dec 2024
Is this the analysis of the primary completion data?*	Yes
Global end of trial reached?*	Yes
Global end of trial date*	2 NOV 2023
Was the trial ended prematurely?	No

General information about the trial

Main objective of the trial*: *Enter a description for the mail objective(s) of the trial*

The aim of this study is to test the efficacy and safety of a suboptimal quantity of pancreatic islet transplantation associated with transient immunosuppressive/modulatory treatment for the treatment of early type 1 diabetes

Actual start date of recruitment*	closed
Long term follow-up planned*	Yes (5 years completed)
If Yes, rationale:	Safety ☑ Efficacy ☑
Duration of trial	8 Years
Independent data monitoring committee (IDMC) involvement?*	No
Protection of trial subjects*:	Yes
Background therapy:	
Evidence for comparator:	

Population of trial subjects

Subjects enrolled per country

Country:	ITALY
Planned number of subjects	6
Actual Number of subjects enrolled*	10 screening; 6 treated and completed
Worldwide total number of subjects	NA
EEA total number of subjects	

Subjects enrolled per age group

In utero*	
Preterm newborn - gestational age < 37wks*	
Newborns (0-27 days)*	
Infants and toddlers (28 days-23months)*	
Children (2-11 years)*	
Adolescents (12-17 years)*	
Adults (18-64 years)*	6
From 65 to 84 years*	
85 years and over*	

Subject disposition

Recruitment details: *Enter key information relevant to the recruitment process for the trial (eg gates of recruitment period and territories)*

Italian patients with newly diagnosed type 1 diabetes attending outpatient clinics at participating center were enrolled and treated within 6 months of their initial diagnosis. Recruitment focused on identifying eligible patients soon after diagnosis to allow for timely intervention. The process involved screening outpatient records and referrals across multiple Italian regions to ensure a representative sample of newly diagnosed individuals suitable for the trial.

Pre-assignment - *Screening details*: *Enter relevant information related to screening (eg screening criteria, significant events and approaches)*

Screening Criteria

- Recent Diagnosis:
  Patients must have been diagnosed with type 1 diabetes within the previous 180 days (6 months).
  In specific cases, eligibility may be extended up to 2 years from diagnosis.
- Age:
  Participants must be adults (18 years or older).

Pre-Transplant Monitoring

During the waiting period for suitable tissue for transplantation, enrolled patients are required to return periodically for reassessment to ensure they continue to meet inclusion criteria.
If, after 6 months from disease onset, transplantation has not been possible, the patient is excluded from the study.

Period 1

Period title*	Overall Trial
Is this the baseline period?	Yes or No
Allocation method*	Non-randomised – controlled ☑
Blinding used*	Not blinded ☑

Arms

Arm title*	***Single arm***
Arm description:	
Arm type*	Experimental
Investigational medicinal product name*	Islet of Langerhans, Thymoglobulin, rapamycin, Pegfilgrastim
Investigational medicinal product code	
Other name	
Pharmaceutical forms*	Cellular tissue, Tablets (rapamycin), powder in vial to be reconstituted (Thymoglobulin), pre-filled syringe (Pegfilgrastim)
Routes of administration*	intrahepatic infusion via portography (Cellular tissue), oral (rapamycin), intravenous (Thymoglobulin), subcutaneous (Pegfilgrastim)
Dosage and administration details*	1500 EIQ/Kg; Rapamycin 0.1 mg/kg; Thymoglobulin 6 mg/kg; Perfilgrastim 6 mg x six doses every 2 weeks starting from the end of the ATG infusion

Number of subjects in period	Arm Title (overall population)	Arm Title *(repeat for each arms if applicable)*
Started*	6	
Completed*	6	
Subject non-completion reason (if applicable)	0	
AE, non fatal	19	
AE, fatal	0	
Consent withdrawn by subject	3	
Lack of efficacy	0	
Lost to follow up	0	
Physician decision	0	
Pregnancy	0	
Protocol Deviation	0	
Other		

Baseline characteristics

Reporting groups* Overall cohort	
Reporting group title*	recruited
Number of subjects at the baseline*	10

Reporting group description: *You can report per arm in the baseline period or for the overall baseline period*

10 Patients enrolled before any treatment assignment; 6 patients treated

Subject analysis sets

Add a subject analysis set if you wish to report on groups different from the reporting group defined above (repeat if applicable)

Subject analysis set title*	*Treated*
Subject analysis set type*	Full Analysis
Subject analysis set description*	*The patient which received the islets transplantation*
Number of subjects in subjects analysis set*	*6*

Age characteristics*

Complete either the age categorical, age continuous or complete both these characteristics in order to collect values for the reporting groups and optionally the subject analysis sets.

	Characteristic title*	Units*	Age categories*
Age categorical	Age group	year	18-65

	Characteristic title*	Units*	Central tendency*	Dispersion type*
Age continuous	Year	Years	28.2	18-43

Gender characteristics*

	Characteristic title*	Units*	Gender categories*
Gender categorical	Sex	subject	Female 6 Male 4

Study specific characteristics

	Characteristic title*	Units *	Categories*	Number of subject for each categories
Study specific categorical				
Study specific categorical				
Study specific categorical				
Study specific categorical				
Study specific categorical				

End points

Add subject analysis set if you wish to report on groups different form reporting groups defined above

Subject analysis set title*	treated
Subject analysis set type*	Full Analysis
Subject analysis set description*	Patients who underwent the intervention
Number of subject in subject analysis set *	6

End points definitions

End point title*	Change from baseline in insulin secretory response assessed as 2-hour area under the curve (AUC) of plasma C-peptide in response to mixed meal (MMTT) one year after transplantation	
		Values
Countable or measurable?*	Stimulated C-peptide AUC (120m)	Pre: 268 ng/ml Week 52: 203 ng/ml Year 5: 110 ng/ml
If countable, Countable units*:		
If measurable, Measurable units*	ng/mL per 120m	
Measure type*:	Median	
Precision/dyspersion type*	Range	

End point type*	Primary

End point timeframe*:
Baseline, Week 52, Year 5

Use categories only if the data for the end point can be categorized

Category title

Specify the groups of subjects applicable to this end point

Reporting groups*	NOT APPLICABLE		
Period			
Arms			
subject analysis sets			

Adverse events

Adverse events information

Timeframe for reporting adverse events*:
AE assessment was done at each visit or contact with the subject

First patient first visit: 22 APR 2015
Last recruitment date: 12 APR 2018
Study closure: 02 NOV 2023

Adverse event reporting additional description: *Enter information about the AE collection and provide details about the method of assessment and monitoring*
AE monitoring was systematic and occurred at each study visit or patient contact. All AEs were recorded and categorized according to CTCAE v3, with special attention to treatment-emergent events during and following immunosuppressive therapy and islet infusion. Monitoring included laboratory testing, physical examination, and patient-reported symptoms.

Assessment type*	Systematic
Frequency threshold for reporting non-serious adverse events*	*ANNUAL*

Dictionary used

Dictionary name*	CTCAE
Dictionary version*	V. 3

Adverse events reporting group definition

Use arms from baseline period as reporting groups
OR

Reporting group title*: *Overall cohort*

For this reporting group, provide the following totals:

Subject exposed*	6
Subjects affected by non -SAE*	6
Total number of deaths (all causes)*	0
Total number of deaths resulting from adverse event*	0

Serious adverse event details and values

System organ class*:

Event term*:

Values for serious adverse event per reporting group *

Reporting groups	Subjects affected number	Subjects exposed number	Occurrences all number	Occurrences causally related to treatment number	Fatalities number	Fatalities causally related to treatment number
IMP side effects	3	6	3	NA	0	0
Side effects infusion procedure	1	6	1	NA	0	0

Serious Adverse Event Details and Values

System Organ Class*	Event Term*	Subjects Affected	Subjects Exposed	Occurrences All	Causally Related to Treatment	Fatalities	Fatalities Causally Related
Investigations	Transient transaminitis	3	6	3	Not applicable (NA)	0	0
Skin and subcutaneous tissue disorders	Rash (mild, self-resolving)	1	6	1	NA	0	0

Values for non-serious adverse event per reporting group*

Threshold for non-serious adverse event reporting is:

Reporting groups	Subjects affected number	Subjects exposed number	Occurrences all number
IMP side effects	6	6	6
Side effects infusion procedure	1	6	1

Non - Serious adverse event details and values

System organ class*:

Event term*:

Non-Serious Adverse Event Details and Values

System Organ Class*	Event Term*	Subjects Affected	Subjects Exposed	Occurrences All
Investigations	Transient leukopenia	6	6	6
Immune system disorders	Mild systemic symptoms (fever, myalgia, lymphadenopathy)	1	6	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol*? Yes

Date	Amendment
24 apr 2015	Inclusion criteria: he study was extended to a population of patients with T1D onset after 180 days but within two years provided that residual secretory function was evident, quantified as the presence of C peptide under stimulation with MMTT > 0.3 ng/ml; corrected the incorrect definition of phase I/II study which is actually phase II
18 aug 2016	extension of follow up from 12 months to 5 years; increase in the overall number of patients enrolled in the study at screening in order to reach the goal of 6 transplanted patients

Notes:

Interruptions (globally)

Were there any global interruptions to the trial*? No

If Yes, Interruption date

Interruption descrption

Limitations and caveats

None reported

Online references

Enter PubMed identifier (PMID)

PMID: .....