IMPACT trial – an INNODIA-endorsed study: status at end-of-recruitment and population baseline characteristics

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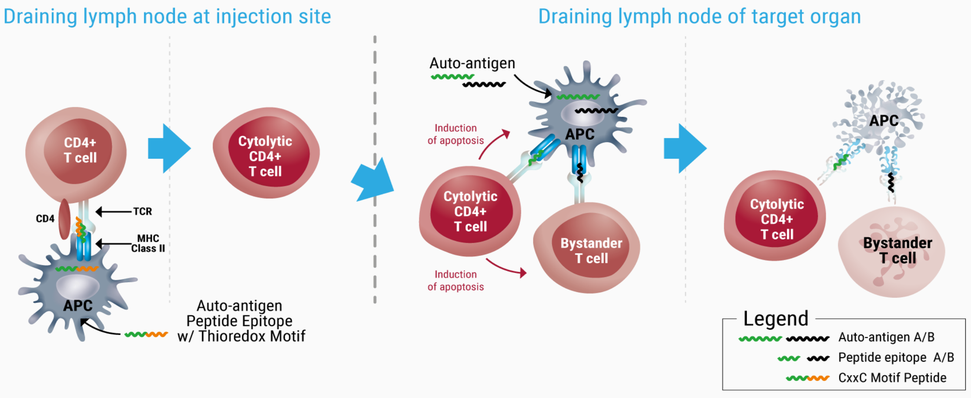
INTRODUCTION

Imotopes™ are linear synthetic peptides combining a sequence of a Human Leukocyte Antigen (HLA) class II T cell epitope from an autoantigen which is causally associated to a given immune-mediated disease, with a thioredox motif which has oxido-reductase activity.



Subcutaneous injection with Imotopes™ generates cytolytic CD4 T cells (cCD4) capable of inducing apoptosis of antigen presenting cells involved in the disease pathway along with cognate pathogenic T cells responsible for tissue inflammation and damage. By nature, Imotope™-induced cCD4 are highly specific, thereby halting the autoimmune attack while leaving the rest of the immune system intact.

IMCY-0098 is an Imotope™ being developed for Type 1 diabetes (T1D) based on insulin sequence and designed to bind HLA-DR3 and DR4. The first clinical trial demonstrated IMCY-0098 has an excellent safety profile. In addition, treatment-specific cCD4 T cells were detected for the first time in humans, along with a concomitant decrease of effector T cells involved in the disease mechanism of T1D. Finally, a preliminary promising clinical response was observed together with positive trends on clinical endpoints and immune findings supporting the design of the IMPACT trial presented here.

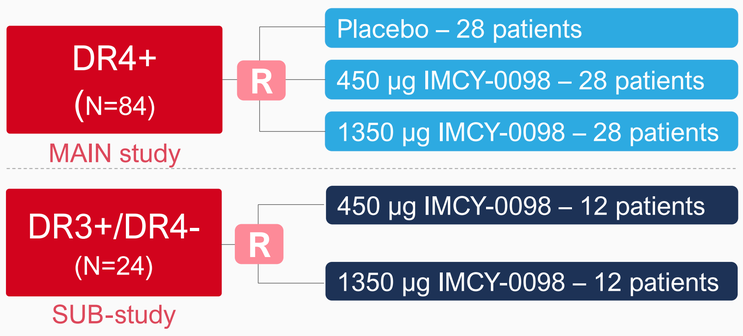
STUDY OVERVIEW (NCT04524949)

Main trial objectives

- Demonstrate **preservation of C-peptide** after 1 and 2 years
- Characterise the **immune response** induced by the treatment
- Confirm the **good safety profile** reported in the phase 1 study

Study design

Treatment arms: Placebo + 2 dose levels of IMCY-0098
Follow up: 2 years from randomisation (primary analysis at 1 year)
Target recruitment: 84 Patients in the main study & 24 in the sub-study
8 countries: Australia, Belgium, Sweden, Lithuania, Italy, Slovenia, United Kingdom and United States
In collaboration with INNODIA and T1D UK consortia

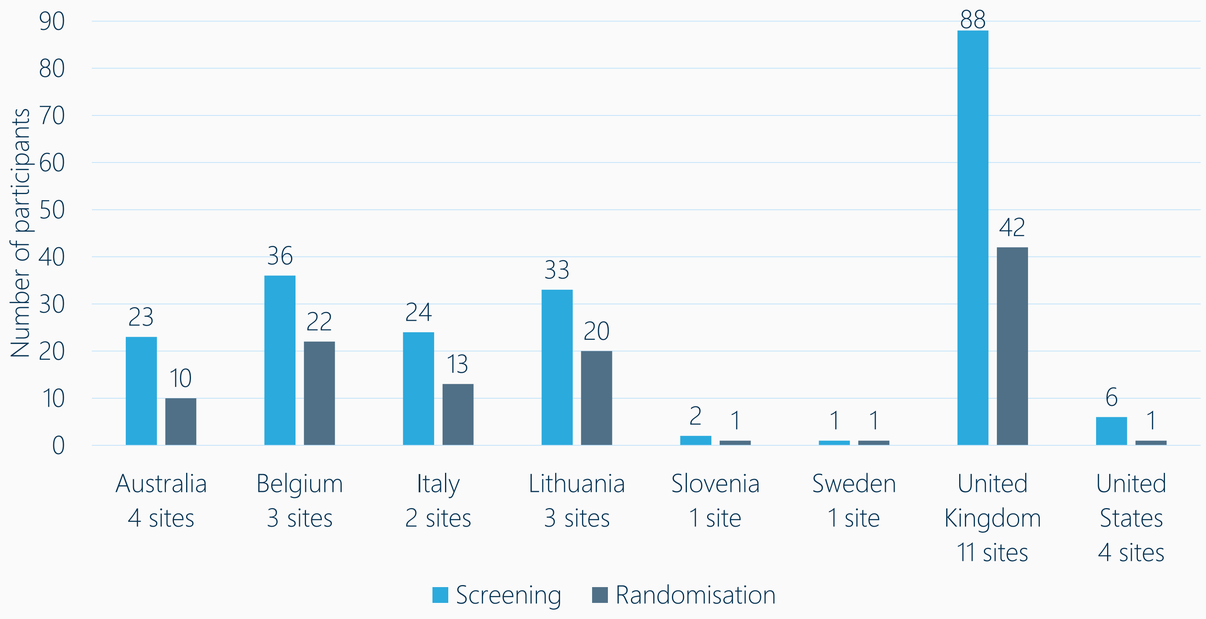


Inclusion criteria

- HLA-DR4+ for the main study
- HLA-DR3+/DR4- for the sub-study
- 18 – 45 years of age
- Initial diagnosis of T1D within 9 weeks before study start
- Random C-peptide levels ≥200 pmol/L
- Positivity for at least 1 T1D-related autoantibody (GAD65, IA-2 or ZnT8)

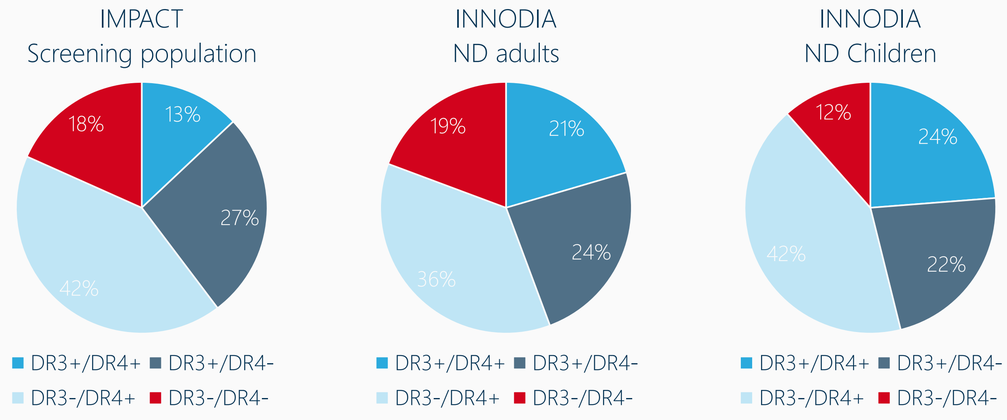
RECRUITMENT PERFORMANCE

Recruitment was conducted between October 2020 and February 2023 in a total of 29 sites from 8 countries and 3 continents. 86 DR4+ and 24 DR3+/DR4- newly diagnosed (ND) adult T1D patients were recruited. To achieve the recruitment target, 213 patients were screened. The main reasons for screen failure were the HLA status (55%) and the absence of T1D-related autoantibodies against GAD65, IA-2 or ZnT8 (31%). Patients are currently followed up to 48 weeks for the primary analysis of the study.



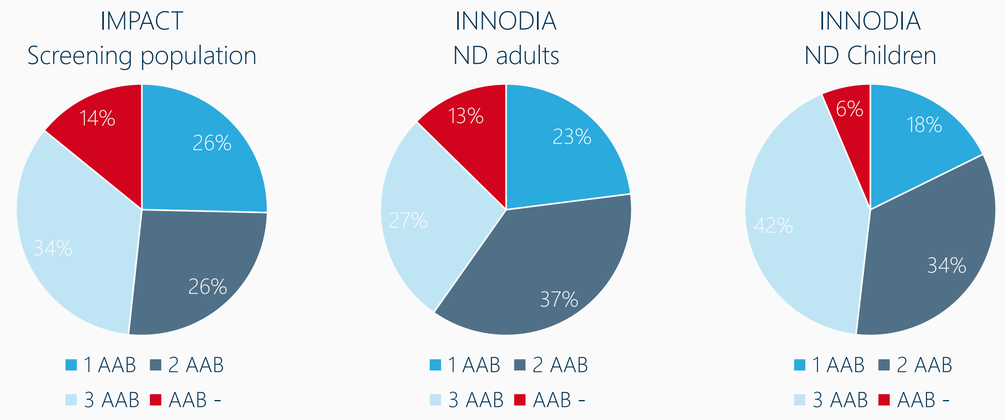
HLA DISTRIBUTION

MHC Class II specificity is a key component of the Imotope approach. IMCY-0098 was designed to be a good binder for the two major HLA associated with T1D, namely DR3 and DR4. Screening population of the IMPACT trial was compared with adult and children population in the INNODIA natural history study. All population showed comparable distribution of HLAs.



AUTOANTIBODIES DISTRIBUTION

Detection of islet autoantibodies (GAD65, IA-2 and ZnT8) is a key component of T1D diagnosis. This parameter was compared across populations of IMPACT and INNODIA natural history studies. A similar distribution was observed between groups, except for a lower proportion of triple-negative patients in ND children of the INNODIA study as observed in previous studies.



BASELINE CHARACTERISTICS

Study baseline characteristics (age, gender, baseline C-peptide and baseline HbA1c) from the IMPACT trial were compared with data from ND participants (adults 18-45 y.o. and children 1-17 y.o.) from INNODIA natural history study (NCT03936634). All parameters presented similar distributions across the different study populations except for C-peptide which showed a lower level in ND children of the INNODIA study in line with the accelerated disease progression in this population.

	IMPACT screened	IMPACT randomised	INNODIA ND Adults	INNODIA ND Children
Nbr of participants	213	110	92	525
Age (mean (SD))	28,11 y.o.(6,83)	27,87 y.o.(6,85)	28,39 y.o.(7,11)	9,16 y.o.(4,27)
Gender (frequency (%))	Female = 89 (41.8%) Male = 124 (58.2%)	Female = 55 (50%) Male = 55 (50%)	Female = 32 (34,72%) Male = 60 (65,22%)	Female = 229 (43,6%) Male = 296 (56,4%)
C-peptide AUC MMTT (mean (SD))	/	V0: 998 pmol/L (440,3)	V2: 1049 pmol/L (652)	V2: 825 pmol/L (551)
HbA1c (mean (SD))	V1: 8,44% (1,70) /	V1: 8,30% (1,66) V2: 6,98% (1,09)	V1: 8,90% (1,67) V2: 6,53% (0,82)	V1: 8,94% (1,75) V2: 6,68% (0,89)

CONCLUSION

The IMPACT study and INNODIA natural history study have recruited participants with similar baseline characteristics and T1D parameters allowing further comparisons and analyses, including support in design of future paediatric studies, once clinical trials will be completed.

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