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Phase Ib clinical trial of T1D-Imotope^{TM} in patients with recent-onsent Type-1 Diabetes

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Abstract:
Background and aims: Type 1 diabetes is an auto immune disease whereby pancreatic beta cells are destroyed by effector CD4 and CD8 T cells. No curative treatment exists. T1D-Imotope^{TM} (IMCY-0098) is an innovative immunotherapeutic technology, consisting of a synthetic peptide containing an MHC class II epitope of proinsulin linked to a thioredox motif. In a NOD mouse model, injection of a murine T1D-Imotope^{TM} prevents and stops disease development through induction of cytolytic CD4 T cells that leads to apoptosis of antigen presenting cells and effector T cells activated against beta cells auto antigens. IMCY-0098 is expected to be disease-modifying by stopping the autoimmune-mediated destruction of beta cells in the pancreas through an antigen-specific mechanism of action whilst preserving overall immune competence of the diabetic patients. The safety, clinical efficiency and immune responses induced by IMCY-0098 treatment were evaluated in a phase Ib clinical trial in recent-onset adult T1D patients.
Materials and methods: Patients, aged 18-30y, diagnosed ≤6 months with type 1 diabetes, treated with insulin but with fasting C-peptide at screening > 0.2nmol/L, HLA-DR3 and/or DR4 positive were recruited into three sequential cohorts (increasing doses) to receive IMCY-0098 or placebo in a 3:1 randomization ratio. IMCY-0098 was administered SC with alum as adjuvant. In total, 8 visits were scheduled per patient during a 6-month-period. Mixed meal tolerance tests were performed at screening, week 12 and week 24 and the daily doses of insulin treatment were recorded. PBMCs were collected to analyse transcriptomics profile and to measure IMCY-0098 specific cytolytic CD4 response and (pancreatic) beta-cells antigen specific effector T cell responses by flow cytometry.
Results: 41 patients were recruited (cohort 1: n=8, cohort 2: n=12 and cohort 3: n=21) and all received 4 injections of IMCY-0098 or placebo and were followed up for 6 months. At the time of submission of this abstract, all visits are nearly completed and no patient drop-out has been reported. An independent DSMB reviewed data twice to allow dose escalation and indicated that there were no safety concerns. In the below table, a safety overview of the study and per cohort is given in a blinded manner.

BLINDED SAFETY SUMMARY						
	Adverse Events					SAE***
	Grade 1	Grade 2	Grade 3	Solicited*	Possible/Probable**	Cases
Cohort 1	96%	2%	2%	44%	46%	0
Cohort 2	79%	21%	0%	44%	43%	1
Cohort 3	81%	19%	0%	58%	51%	1
Overall	**83%**	**16,6%**	**0,4%**	**48%**	**47%**	
*Solicited AE predefined in the protocol and collected up to the 7th day after each injection. 67% of local injection site reactions and 33% systemic AE. Mild in 88% of the case and moderate in 12%. No severe cases.						
**Mild in 87% and moderate in 12% of the cases. One case was reported as severe in cohort 1.						
***1 planned surgery (unrelated) - 1 event for which relationship cannot be excluded.						

Ultimately, this study will result in identification of signals of clinical and immune activity.
Conclusion: Preliminary safety data are encouraging and suggest that the T1D Imotope^{TM} is safe in patients with recent onset T1D. At the time of submission of this abstract, the clinical study is still blinded. Full study results will be available and presented at the EASD 2019.
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