Diagnostic

A new method for assessing the efficacy of immunotherapies in type 1 diabetes

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Background

Emerging immunotherapy treatments such as anti-CD3+ antibodies (Abs) to prevent type 1 diabetes (T1D) require novel diagnostic methods to identify immunotherapy responders and to predict disease onset in pre-diabetic patients. For the past 3 decades HLA-DR haplotypes and serum islet autoantibodies have been used to calculate T1D risk but have limited precision to predict time to diagnosis, or response to therapy.

Description of the Invention

The Danska lab has developed a new method to identify responders/non-responders to anti-CD3 Abs in T1D at-risk individuals. They assessed Ab responses against a panel of taxonomically diverse intestinal "commensal" bacteria species (anti-commensal Ab; [ACAb]) in serum from clinical study participants treated with anti-CD3 Mab teplizumab (Tzield™) vs placebo. IgG2 responses to 3 commensal species associated with time to T1D diagnosis and Tzield responses that delayed T1D onset.
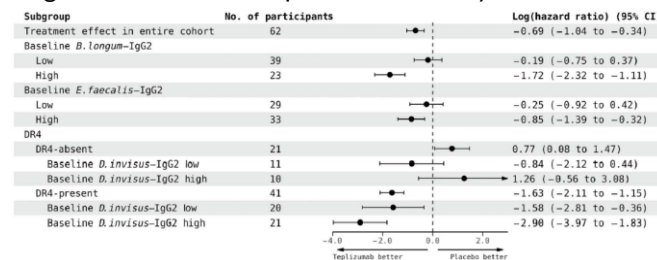
Subgroup	No. of participants		Log(hazard ratio) (95% CI)
Treatment effect in entire cohort	62		−0.69 (−1.04 to −0.34)
Baseline *B. longum*–IgG2			
Low	39		−0.19 (−0.75 to 0.37)
High	23		−1.72 (−2.32 to −1.11)
Baseline *E. faecalis*–IgG2			
Low	29		−0.25 (−0.92 to 0.42)
High	33		−0.85 (−1.39 to −0.32)
DR4			
DR4-absent	21		0.77 (0.08 to 1.47)
Baseline *D. invisus*–IgG2 low	11		−0.84 (−2.12 to 0.44)
Baseline *D. invisus*–IgG2 high	10		1.26 (−0.56 to 3.08)
DR4-present	41		−1.63 (−2.11 to −1.15)
Baseline *D. invisus*–IgG2 low	20		−1.58 (−2.81 to −0.36)
Baseline *D. invisus*–IgG2 high	21		−2.90 (−3.97 to −1.83)

Teplizumab better   Placebo better

Fig.1 Responses to Tzield are associated with IgG2 responses to selected gut bacteria before treatment.

Commercial Applications

These Ab responses are **the first biomarkers** linking human intestinal bacteria with T1D progression. ACAb analysis provides a new approach to identify pre-T1D (stage 2) or new onset (stage 3) T1D patients who may benefit from Tzield, now approved by the U.S. FDA for delaying TD1 onset, or emerging T cell modulators.

Developmental Stage

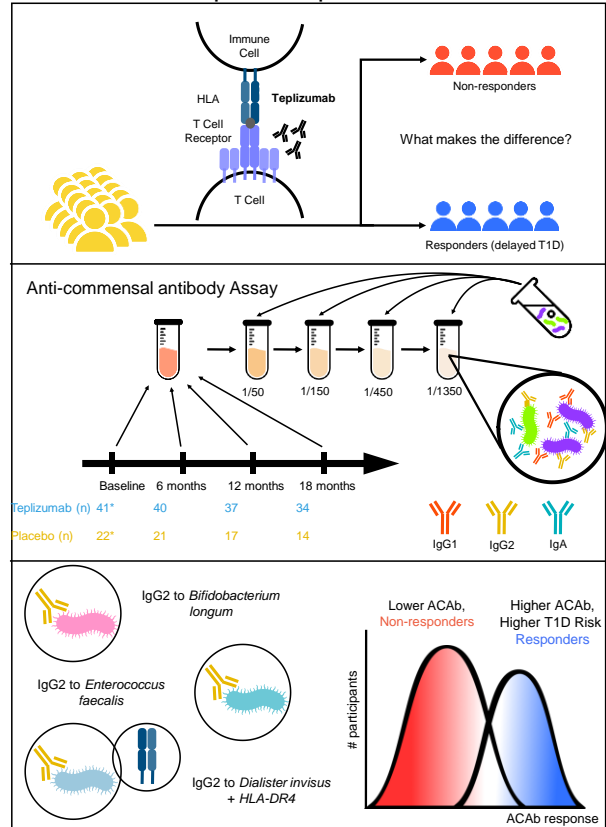Validation on independent patient cohort.

	Baseline	6 months	12 months	18 months
Teplizumab (n)	41*	40	37	34
Placebo (n)	22*	21	17	14

Fig.2 Experimental design for ACAb response.

Publication

Patent Status

PCT APPLICATION *Methods for stratifying subjects with type 1 diabetes for treatment with an anti-cd3 antibody and for predicting progression to type 1 diabetes* #PCT/CA2024/051396 filed on 10-24-2024 (currently unpublished).

IP&C is seeking a collaboration to develop and commercialize the new diagnostics platform.

Keywords: Type 1 Diabetes, Anti-CD3 Therapy, Gut Microbiota, Biomarkers, Immunotherapy Response

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