Background-Type 1 Diabetes Consortium (T1DC)

- Issue/Need statement: Currently no therapies are approved for the delay or prevention of type 1 diabetes (T1D)

- Solution: Qualification with FDA and EMA **of islet autoantibodies (AAs) as enrichment biomarkers for use in T1D prevention clinical trials** to enable proper patient selection in clinical investigations of earlier interventions in T1D, allowing:
  - Sponsors of drug development programs to have confidence incorporating biomarkers into their trial designs
  - Regulatory authorities to have confidence relying on biomarkers during their review process
  - Aid the development of therapies and the design of clinical trials to delay and ultimately prevent clinical diagnosis

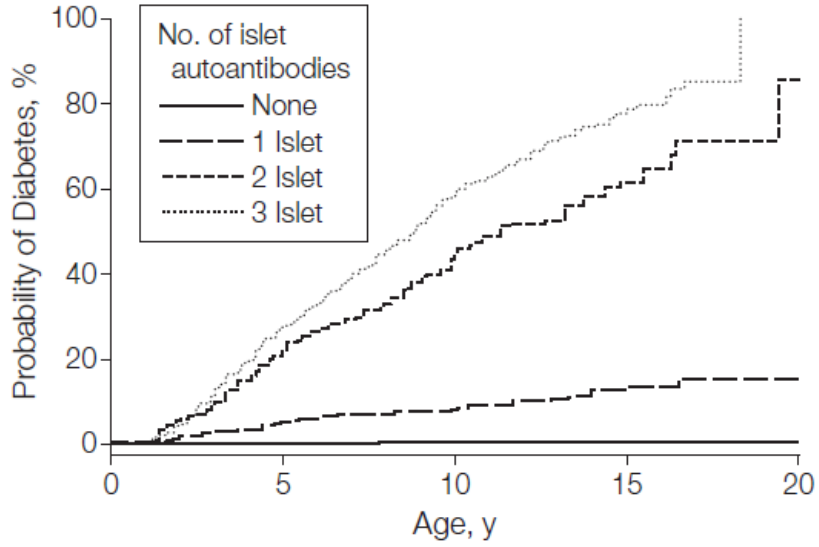
- Goal of T1DC:
  - Develop a model from patient-level data that will quantitatively describe the relationship of the islet AAs and other relevant patient features to the probability of a T1D diagnosis during the course of T1D prevention clinical trials
  - Qualify the islet AAs as enrichment biomarkers to identify subpopulations at highest risk of a T1D diagnosis in T1D prevention trials

Background-T1DC membership

T1DC is a public-private-partnership currently composed of the following Industry and Foundation Members, Academics, and Observers/Advisors:

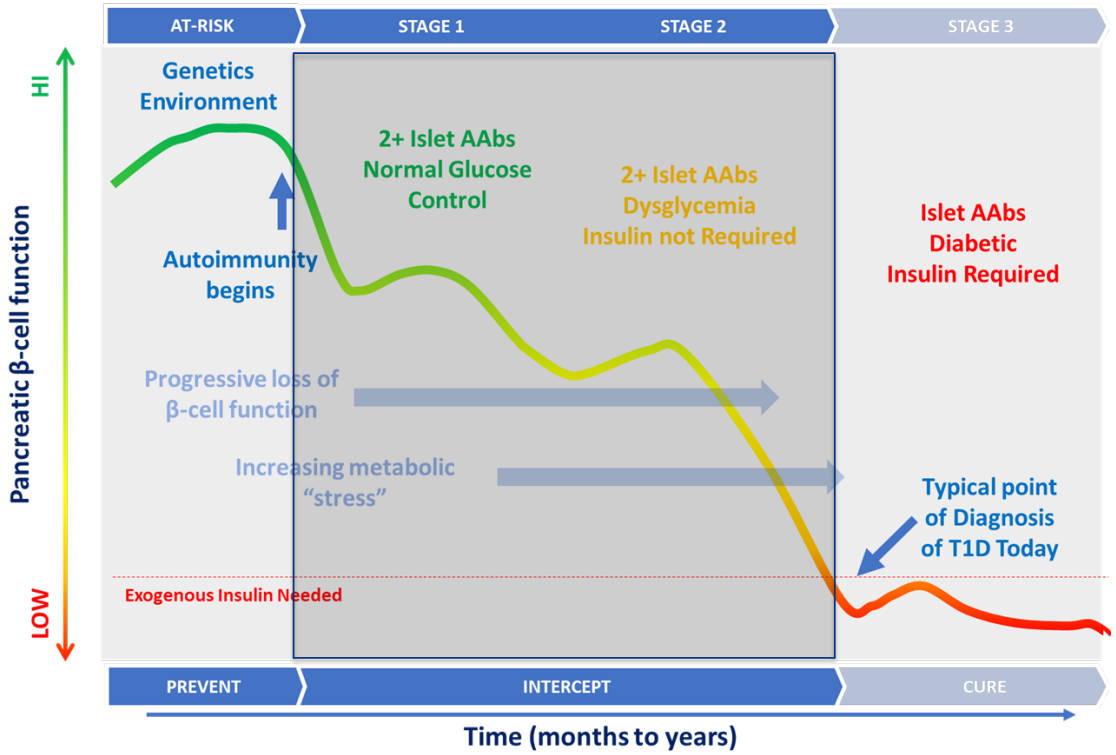
- Janssen
- JDRF
- Helmsley Trust
- Novo Nordisk
- Provention Bio
- Benaroya Research Institute
- Helmholtz Zentrum München
- Lund University, Sweden
- University of Bristol
- University of Colorado Denver
- University of Florida
- University of Helsinki
- University of Leuven
- University of Munich
- University of Oulu
- University of Tampere
- University of Turku
- FDA
- NIH
- INNODIA

Autoantibodies are the Foundation for Staging[1] of Presymptomatic T1D



No. at risk
Islet autoantibodies, No.

3 Islet	358	250	112	20	
2 Islet	227	168	82	19	1
1 Islet	474	430	272	118	9
None	12 318	8875	5253	1161	44



Ziegler et al., *JAMA* (2013): 2473–79.

[1]Diabetes Care 2015 Oct; 38(10): 1964-1974

But we are running trials today using autoantibodies…

- Provide valuable information to reduce uncertainty in regulatory decisions
  - Approving an investigatory trial that will expose even a few hundred people to risk is a very different proposition for regulators than approving a drug that will possibly be used in tens of thousands for years to come
  - It is vital that, when we can, we provide regulators with the body of evidence that removes uncertainty for them, particularly when considering medicines for children

- Enable the FDA/EMA as partners
  - The regulators want to enable progress and desire to be in the best possible position to help all of us achieve that for patients
  - Providing the regulators with data in the form that they need enables a deeper understanding of the disease and greater confidence that new medicines will have appropriate risk: benefit
  - A qualified biomarker can serve as the foundation upon which future biomarkers may stand

Challenges/Considerations for Qualification

- Three biggest challenges are data, data, and data
  - Who has it?
  - What does it take to get it?
  - How fit for purpose is it (appropriate, complete, validated?)
- Precision in the Context of Use Statement
  - Understand what the data can support and don't overreach
  - Keep the long goal in mind
  - Make it as easy as possible for the regulators to agree to qualification
- Keep focused on implementation
- Qualification is the main goal, but there are other benefits
  - Deeper understanding of disease "subtypes"
  - Tools that can aid in clinical development/trial planning

Value to Stakeholders

Endorsed model supporting the islet AAs as enrichment biomarkers for T1D = **Drug Development Tool (DDT) that can be used with confidence**

- **Patients:**
  - Catalyze risk screening, reduce DKA hospitalizations and means of reimbursement
  - Development of therapies that may delay or ultimately prevent beta cell loss
- **Industry**:
  - Identification of a patient-pool of known trajectory for inclusion in prevention studies
  - Quantitative benefit risk analysis for outcomes assessment and trial duration
  - Knowledge that the regulatory agencies are familiar with and utilizing the same tool
- **Academics:**
  - Translation of the scientific research into drug development
  - Enables the translation of cutting-edge research by providing a regulatory benchmark
  - Integrated database can provide a means for further investigations
- **Regulatory Agencies:**
  - Vetted and approved disease progression tool in T1D for evaluation of sponsor trial data

“The patients are waiting…”

- Paul Janssen

Thank You

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