The Global Platform for the
Prevention of Autoimmune Diabetes

GPPAD SCIENCE-NEWSLETTER

Issue 02/2021

DEAR READER,

Welcome to the second GPPAD Science-Newsletter. In our newsletters, we keep you up to date on the most important developments of our GPPAD projects. If you do not yet know who we are and what we do, then please read our first newsletter. You can find it at this link.

We have two highlights in the newsletter: We have completed recruitment for POInT and started a new primary prevention trial SINT1A.

Feel free to forward the newsletter to others who may be interested. If you have not yet subscribed to the newsletter, please register here.

I hope you enjoy reading the GPPAD Science Newsletter and look forward to having you join us on our journey to a world without type 1 diabetes.

With best regards,

Prof Dr Anette-Gabriele Ziegler
(Director, Institute of Diabetes Research, Helmholtz Zentrum München)

WE RESEARCH. WE DEVELOP. WE FIGHT.

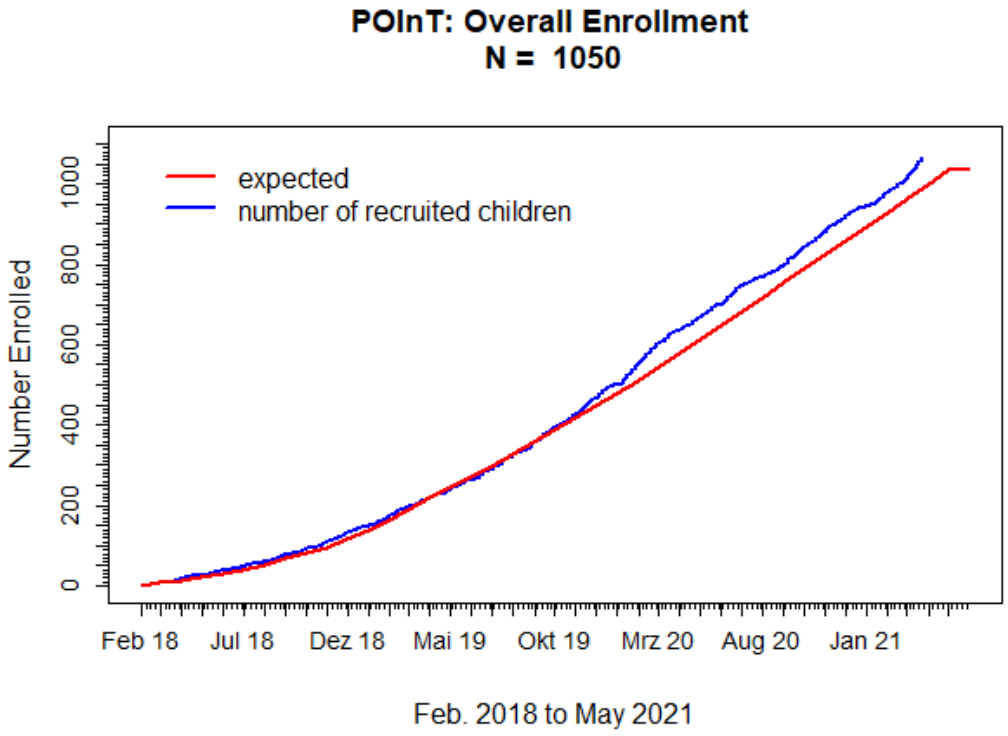
FOR A WORLD WITHOUT TYPE 1 DIABETES.

POINT (PRIMARY ORAL INSULIN TRIAL)

Recruitment completed

A total of **1,050 children** are enrolled in the POInT study at a median age of 6.1 months (range 3.9 – 7 months). Enrollment is complete.

First participant enrolled: 07-Feb-2018
Last participant enrolled: 24-Mar-2021
Enrollment period planned: 3.5 years, Actual ~3.2 years
Projected study end: Jan-2025



Feb. 2018 to May 2021

Participants take the Investigational Medicinal Product IMP (oral insulin or placebo) daily with food until their 3rd birthday, and are followed for 6-54 months after the intervention.

For more information, please refer to the study protocol publication and the overview on clinicaltrial.gov or read our first newsletter.

SINT1A (SUPPLEMENTATION WITH B. INFANTIS FOR MITIGATION OF TYPE 1 DIABETES AUTOIMMUNITY)

Our new study

The GPPAD-SINT1A Study is designed as a randomised, placebo-controlled, double blind, multicentre, multinational, primary prevention study aiming to assess whether daily administration of probiotic *B. infantis* to children with elevated genetic risk for type 1 diabetes in the first year of life reduces the cumulative incidence of beta-cell autoantibodies in childhood. The rational is that correcting dysbiosis in early life by supplementation of a probiotic could help to promote immune tolerance thereby inhibiting the initiation of beta-cell autoimmunity.

Infants aged 7 days to 6 weeks from Germany, Poland, Belgium, UK and Sweden are eligible for study participation if they have a >10.0% expected risk for developing multiple beta-cell autoantibodies by age 6 years as determined by genetic risk score or family history and HLA genotype (for more information refer to our last newsletter and the manuscript on GPPAD-02). Infants are randomized 1:1 to daily administration of *B. infantis* EVC001 or placebo until age 12 months, and followed for a maximum of 5.5 years thereafter. The primary outcome is the development of persistent confirmed multiple beta-cell autoantibodies. Secondary outcomes are 1. Any persistent confirmed beta-cell autoantibody, defined as at least one confirmed autoantibody in two consecutive samples, including IAA, GADA, IA-2A or ZnT8A, 2. Diabetes, 3. Transglutaminase autoantibodies associated with celiac disease, 4. Respiratory infection rate in first year of life during supplementation, 5. Safety. Exploratory outcomes include allergy, antibody response to vaccines, alterations of the gut microbiome or blood metabolome, stool pH and calprotectin.

SINT1A study overview:

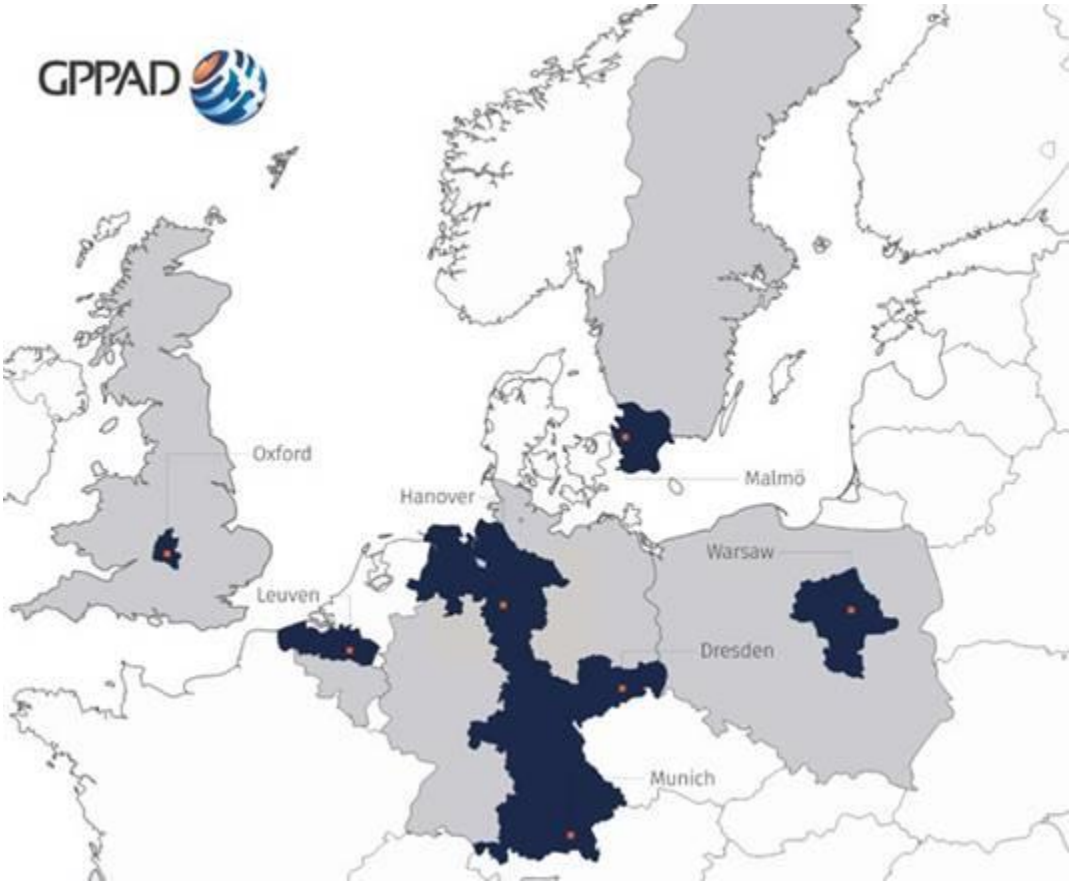
Design: randomised, placebo-controlled, double blind, multicentre, multinational, primary prevention trial
Randomization: 1:1 (B. *infantis* EVC001 or placebo)
Inclusion age: 1-6 weeks

Intervention: B. infantis EVC001
Treatment duration: until 12 months of age
Follow-up: 2.5-5.5 years after intervention
Trial duration: until 2027
Target: 1,144 participants
Dose: daily administration of EVC001 (minimum 8 x 10^9 colony forming units (CFU) per administration) or placebo
Primary outcome: development of persistent confirmed multiple beta-cell autoantibodies

For more information, please refer to the overview on clinicaltrial.gov.

First participant enrolled: 22-Apr-2021
Participants enrolled by 31-Aug-2021: 78

PARTICIPATING SITES



Dresden (Saxony & Thuringia): Ezio Bonifacio & Reinhard Berner
Hanover (Lower Saxony): Olga Kordonouri & Thomas Danne
Leuven (Flanders): Kristina Casteels
Malmö (Skane): Helena Elding Larsson & Markus Lundgren
Munich (Bavaria): Anette-Gabriele Ziegler & Christiane Winkler
Oxford: Matthew Snape & Manu Vatish
Warsaw: Agnieszka Szypowska & Mariusz Ołtarzewski