View Abstract

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TITLE: NLRP3 Inflammasome Inhibition With Dapansutrile in Type 2 Diabetes and Elevated Systemic Inflammation: Rationale and Design of the DAPAN-DIA study

PRESENTATION TYPE: Oral or Poster

CURRENT COMMUNITY: 19. Cardiometabolic Health and Diabetes

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Abstract Body (Do not enter title and authors here): Background: Monoclonal antibodies against IL-1β decrease inflammation, improve insulin secretion and glycaemia, and reduce residual CV risk, but must be injected and are associated with higher incidence of fatal infection. There remains an unmet need for an oral treatment for T2D patients at risk for cardiometabolic complications to safely reduce IL-1β-mediated inflammation chronically & with low risk of immunosuppression. In an initial dose-range finding study in heart failure patients with T2D, we reported evidence of anti-hyperglycaemic efficacy and improvement in LVEF with dapansutrile an oral specific inhibitor of the NLRP3 inflammasome.

Objectives: To investigate the potential of preventing the transition to organ complications, The EU funded consortium INTERCEPT-T2D in collaboration with US based biotech Olatec Therapeutics has launched a clinical trial of anti-inflammatory therapy with dapansutrile targeting T2D patients with low-grade inflammation.

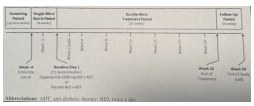
Methods: Dapansutrile in Diabetes and Complications (DAPAN-DIA, NCT06047262) aims to determine whether NLRP3 inhibition with dapansutrile has the potential to not only improve glycaemia but also reduce micro- and macro-vascular risk and complications from diabetes. DAPAN-DIA is a multicenter, pbo-controlled, prospective, randomized, double-blind trial conducted in Switzerland, France, Belgium and Germany. A total of 300 patients with T2D, HbA1c >7.5% and hsCRP>1.5 mg/L are being randomized to either dapansutrile 1000 mg BID or matching PBO tablets for 6 months (2:1 ratio dapansutrile: pbo). The primary endpoint is change from baseline HbA1c. Secondary endpoints include biomarkers associated with diabetic complications, progression of MASLD as well as chronic inflammation (IL-1 β, IL-6 and hsCRP). A subject-assessed QoL questionnaire is also collected.

To detect an absolute difference of 0.5% in HbA1c between groups, approximately 300 subjects will be randomized 2:1 ratio to achieve 80% power, assuming a standard deviation of 1.2% in change from baseline in HbA1c at week 26.

Results: The trial has launched and currently is enrolling subjects.

Conclusions: DAPAN-DIA is the first placebo-controlled, adequately powered, large, multi-center study with an oral NLRP3-specific Inhibitor, dapansutrile. The trial will generate important data on a new clinically relevant dimension in T2D care where consideration at diagnosis of inflammatory parameters are of importance for the transition to T2D-related complications.

KEYWORDS: Cardiovascular health, Diabetes (Type II), Insulin resistance, Cardiometabolic health, Inflammation and inflammatory markers.



DAPAN-DIA Trial Schematic

Abstract Graphic/Image Description: DAPAN-DIA Trial Schematic., No Image, No Image