Name of Sponsor: ParaTech A/S	
Name of Finished Product: TSO 7500	
Name of Active ingredient: *Trichuris suis* Ova (TSO)	
Title of study: *Pro*biotic Treatment of Ulcerative Colitis with *Trichuris suis* ova (TSO) (PROCTO)	
Investigators: PI: Andreas Munk Petersen, MD, PhD Sub investigators: Michelle Vernstrøm Prosberg, MD and Johan F.K.F. Ilvemark, MD	
Study center(s): Hvidovre Hospital, The Gastro Unit, Kettegård Allé 30, 2650 Hvidovre	
Publication (reference): N/A	
Studied period (years): 3.5 years First enrolment 18.06.2018 Last enrolment 25.06.2021	Phase of development: Phase 2b
Objectives: To demonstrate that administration of 7500 TSO every second week over 24 weeks will reduce the intestinal inflammation in moderate Ulcerative Colitis by achieving clinical remission by full Mayo disease score (primary endpoint).	
Methodology: Double-blind randomized, placebo-controlled, 24-week, comparative, single center, exploratory phase II proof of concept trial.	
Number of patients: 120 patients planned and 119 patients enrolled	
Diagnosis and main criteria for inclusion: Established diagnosis of Ulcerative Colitis confirmed by endoscopic (sigmoidoscopy) and histological criteria, at least 3 months prior to inclusion. Disease extension corresponding to E2 (left side colitis) or E3 (extensive colitis) according to the Montreal Classification, i.e., at least 15 cm from anal verge, confirmed by an index sigmoidoscopy.	

Mayo-score between 6 and 10 and including 6 and 10 corresponding to moderately active disease. Calprotectin ≥ 250 µg/g and an endoscopic Mayo score ≥ 2. No treatment or if treated with 5-Aminosalicyl acid (5-ASA): 5-ASA ≥ 8 weeks with a stable dose for at least 4 weeks both oral and rectal use. Tapered down from last oral steroid ≥ 4 weeks ago.
Test product, dose, and mode of administration, batch number: 7500 TSO administered orally (batch no. B2610)
Duration of treatment: 24 weeks
Reference therapy, dose, and mode of administration, batch number: None
Criteria for evaluation: Efficacy Long-term efficacy is evaluated as clinical, endoscopic and symptomatic remission Short-term efficacy is evaluated as symptomatic remission Response is evaluated as reduction of full Mayo score Time to reach effect is evaluated as pMayo remission and response and to symptomatic remission Difference in pMayo over time is evaluated from 12 to 24 weeks Safety Safety is evaluated as related and un-related AE rates as well as SAE rates
Statistical methods: Chi-squared or Fischer's exact test is used to test the difference between the proportion of patients in the TSO and placebo group, who reached the endpoint. Difference in mean time to reach endpoint is analyzed by t-test or by Wilcoxon sum-rank test when normality assumption cannot be satisfied. Difference in mean pMayo over time is analyzed by mixed linear regression model Difference in AE/SAE rates between active and placebo is analyzed by Poisson regression model.
Summary – Conclusions Without steroid co-treatment, TSO seems to generally improve the symptoms of moderate ulcerative colitis after 12-22 weeks of treatment, but the primary end point of full Mayo remission at 24 weeks of treatment was not reached.

The statistical power of the study was compromised by the frequent use of steroids and by a very high placebo effect.

Efficacy Results:

The primary endpoint was not reached as there was no significant difference between the proportion of patients in the TSO and placebo treated groups reaching full Mayo remission. Significant differences between TSO and placebo treatment were found in two secondary endpoints, where the effect of TSO was assessed as symptomatic remission and as pMayo remission in the complete steroid free population from 12 to 22 weeks. This superiority of TSO in improving UC symptoms is supported by indications of lower mean Fecal calprotectin levels and by the significant IBD disability index results at week 24 in the complete steroid free population.

Safety Results:

The majority of AEs are symptoms of background disease, ulcerative colitis and none of the SAEs and AEs raise any safety concerns.

Conclusion:

The primary endpoint was not reached as there was no significant difference between the proportion of patients in the TSO and placebo treated groups reaching full Mayo remission at withdrawal or 24 weeks in either the ITT population or the PP population.

There are indications of a negative effect of concomitant steroid on TSO which may influence the efficacy data in the ITT and PP population.
57 patients (48% of the ITT) were treated with steroid and of these 39 patients (68%) started at visit 1 and 14 patients (25%) started at visit 2, thus the CSF (Complete Steroid Free) population size is reduced below the statistical power calculation.

Significant differences between TSO and placebo treatment were found in two secondary endpoints, where the efficacy of TSO was assessed as symptomatic remission and as pMayo remission in the Complete Steroid Free population from 12 to 22 weeks. A superiority of TSO in improving UC symptoms is supported by the significant IBD disability index results at week 24 in the Complete Steroid Free population.

Overall, the study was compromised by a very high placebo effect e.g., endoscopic remission at week 24 was 41% in the CSF placebo group.

Date of report: 29.11.2022