Safety, tolerability and pharmacodynamic effects for TPM502

Phase 2a study results for a tolerizing nanoparticle therapy for celiac disease

Summary

TPM502 showed a very good safety profile throughout the study in HLA-DQ2.5+ patients.

TPM502 achieved significant, sustained, and dose-dependent reduction in IL-2 and IFN-γ release by gluten-specific T cells and durable immunomodulation of gluten-specific CD4+ T cells.

Patient-reported outcomes (PROs) indicated dose-dependent reduction of symptoms following a gluten challenge (GC).

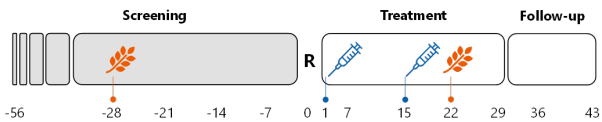
Celiac Disease (CeD) and TPM502

CeD is caused by CD4 T cell responses to gluten peptides in HLA-DQ2.5+ individuals as well as those presenting DQ8+ and DQ2.2+ genetic variants.

TPM502 contains 3 different immunodominant gluten peptides and targets liver sinusoidal endothelial cells (LSECs), antigen-presenting cells capable of inducing immune tolerance.

Trial Design

Phase 2a, double-blind, randomized, placebo-controlled, multicenter study (NCT05660109)

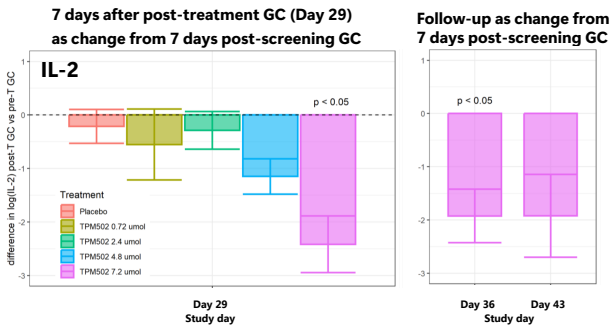


Escalating doses of TPM502 or placebo, administered i.v. on day 1 & day 15 (0.72 µmol, 2.4 µmol, 4.8 µmol, 7.2 µmol cumulative dose)

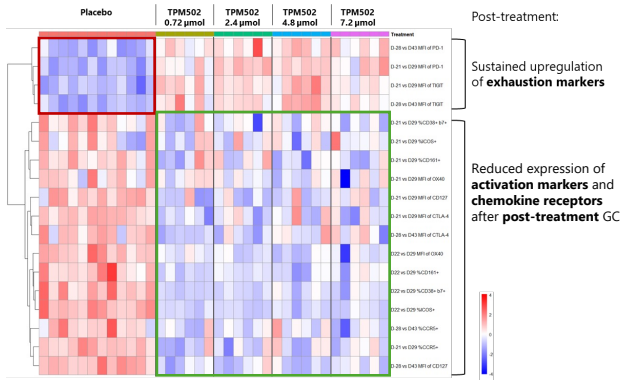
Bolus GC (6g gluten) at screening and 7 days after the last TPM502 administration

Results

1. Significant, persistent reduction of IL-2 and IFN-γ release from gluten-specific T cells following *ex vivo* stimulation with same gluten peptides as TPM502

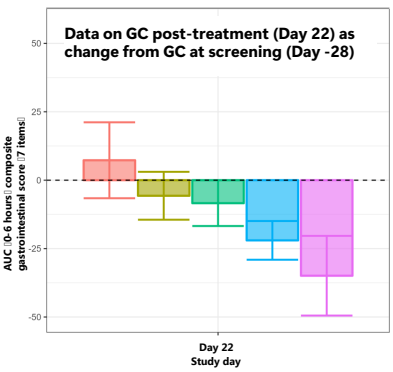


2. Post-treatment phenotypic changes in gluten-specific CD4+ Ttet cells showing regulatory and immunomodulatory effects of TPM502



HLA-DQ2.5 tetramer-based FACS analysis of gluten-specific T cells

3. Assessment of gastrointestinal PROs indicated a dose-dependent reduction in score intensity, accounting for use of anti-emetic/-diarrheal drugs



Conclusion

Based on the positive outcome of this trial, Topas Therapeutics is committed to the further clinical development of TPM502 as a treatment option for celiac disease patients.

In addition, the clinical validation of the Topas nanoparticle technology and therapeutic approach support the company expanding its pipeline into other autoimmune and immune-mediated disease indications.