

PHASE 1/2 DOSE ESCALATION AND DOSE EXPANSION STUDY OF TRANSCON TLR7/8 AGONIST ALONE OR IN COMBINATION WITH PEMBROLIZUMAB IN PATIENTS WITH LOCALLY ADVANCED OR METASTATIC SOLID TUMOR MALIGNANCIES: INITIAL RESULTS FROM DOSE ESCALATION

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Background Resiquimod is a potent TLR7/8 agonist where systemic tolerability limits clinical use. TransCon TLR7/8 Agonist is an investigational prodrug of resiquimod with sustained release intended for intratumoral administration. It has the potential to overcome shortcomings of existing treatments by providing prolonged high local concentrations of resiquimod, promoting potent anti-tumoral responses while reducing systemic drug exposure and treatment related adverse events (TRAEs).¹ The primary objectives of the transcendIT-101 phase 1/2 trial are to evaluate safety and tolerability, and define the maximum tolerated dose and recommended phase 2 dose (RP2D) of TransCon TLR7/8 Agonist, alone or in combination with pembrolizumab.

Methods In dose escalation (3+3 design), patients aged ≥ 18 with advanced solid tumors receive TransCon TLR7/8 Agonist (dose levels: 0.3 and 0.5 mg/injected lesion) as monotherapy or in combination with pembrolizumab. Monotherapy patients receive dosing every 3 weeks (q3w). Combination therapy patients receive staggered dosing in cycle 1 where pembrolizumab is administered 7 days after TransCon TLR7/8 Agonist, then same-day dosing q3w at subsequent cycles. In expansion cohorts, TransCon TLR7/8 Agonist and pembrolizumab are administered same day q3w starting at cycle 1 day 1. Disease is assessed every 9 weeks using Response Evaluation Criteria in Solid Tumors version 1.1, supplemented by pathology, as available. Safety, pharmacokinetics (PK), and pharmacodynamics (PD) are evaluated.

Results As of 27th May 2022, 19 patients enrolled into dose escalation: 9 to monotherapy (3 at 0.3 mg, 6 at 0.5 mg) and 10 to combination therapy (3 at 0.3 mg, 7 at 0.5 mg). All 22 TRAEs were grade 1 or 2 (12 at 0.3 mg, 10 at 0.5mg) with most common TRAEs related to injection site reactions (59%) followed by fever (9%). Preliminary PK results showed low systemic resiquimod C_{max} , with mean systemic resiquimod half-life of 9 days, and no PK interaction with pembrolizumab. PD data from tumor biopsies were consistent with sustained intratumoral upregulation of type I interferon and TLR pathway genes that were comparable across the two dose levels. Preliminary antitumor efficacy was observed, including 1 confirmed partial response (melanoma, monotherapy at 0.3 mg).

Conclusions The transcendIT-101 trial indicates TransCon TLR7/8 Agonist has a well-tolerated safety profile as monotherapy and in combination with pembrolizumab. Results from PD studies demonstrated target engagement that correlates

with observed antitumor activity. While enrollment continues, data support 0.5 mg/injected lesion as the projected RP2D.

Trial Registration NCT04799054

REFERENCE

1. Zuniga LA, Leßmann T, Holten-Andersen L, et al. Intratumoral delivery of TransCon™ TLR7/8 Agonist provides potent anti-tumor activity as a monotherapy and in combination with IL-2 while minimizing systemic cytokine induction. Society for Immunotherapy of Cancer 2019. Nov 6-10, 2019. National Harbor, MD. Poster 676.

Ethics Approval The study protocol was approved by the institutional review board at each participating center. All the patients provided written informed consent.

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