Background: Resiquimod is a potent TLR7/8 agonist where systemic tolerability limits clinical use. TransCon TLR7/8 Agonist is an investigational produg 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).

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 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.

Conclusions: Preliminary PK results showed low systemic resiquimod Cmax 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).

REFERENCES