Background Enrichment of memory B cells, plasma cells and tertiary lymphoid structure is a positive prognostic factor in patients (pts) with a variety of solid tumors,1-3. Designed for systemic administration, TAC-001 is a Toll-like Receptor (TLR) Agonist Antibody Conjugate (TRAAC) comprised of a potent and differentiated TLR9 agonist (T-CpG) conjugated to an antibody against CD22, a receptor restricted to B cells, including tumor-infiltrating B cells. TAC-001 mouse surrogate elicited infiltration of activated B cells, effector T cells and modulation of suppressive myeloid cells within the tumor microenvironment of murine models, including those refractory to anti-PD-1 therapy;4 INCLINE-101 is a first in human Phase 1/2 open-label, non-randomized, dose escalation/dose expansion study to evaluate TAC-001 in pts with advanced or metastatic solid tumors.

Methods In Phase 1, TAC-001 is administered intravenously every two weeks in pts with advanced or metastatic solid tumors. Eligible pts in Phase 1 must have histologically or cytologically documented advanced, metastatic, unresectable malignancies that have progressed on or are intolerant to standard therapy. The Phase 1 study is exploring ascending dose levels of TAC-001 to assess safety, tolerability, efficacy, PK, pharmacodynamics (PD), and identify the maximum tolerated dose (MTD) or maximum administered dose (MAD), and recommended Phase 2 dose (RP2D).

Results As of 20 June 23, 15 pts (median age: 61 yrs) have been treated with TAC-001 (dose ranges from 0.1 to 3.0 mg/kg) intravenously every 2 weeks. Most common treatment related-adverse events include fatigue (n=11, 73.3%), chills (n=8, 53.3%), and pyrexia (n=7, 46.6%). One subject discontinued treatment after two doses due to a DLT of immune-mediated hepatotoxicity (grade 4 elevation of ALT, grade 3 elevation of AST and bilirubin) observed at the 3.0 mg/kg dose level. TAC-001 PK exposures (Cmax and AUC) exhibited dose dependent increase over the dose range tested. Preliminary PD biomarker assessment demonstrated CD22 engagement and internalization by TAC-001 on circulating B cells in subjects across dose levels. TAC-001 mediated activation of B-cells through TLR9 pathway induction has also been demonstrated among subjects across dose levels. Two of eight response evaluable pts have stable disease and remain on study (range 5+ to 10+ months).

Conclusions TAC-001 appears well tolerated with dose dependent PK and PD activity consistent with the proposed proof of mechanism - evaluation & enrollment is ongoing.

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Trial Registration NCT05399654

REFERENCES

Ethics Approval All clinical subjects or participants provided informed consent prior to taking part in this clinical trial. WCG-IRB: IRB Tracking Number: 20222058.