608 RESULTS OF A PHASE 1 STUDY INVESTIGATING CAMIDANLUMAB TESIRINE AS MONOTHERAPY AND IN COMBINATION WITH PEMBROLIZUMAB IN PATIENTS WITH SELECTED ADVANCED SOLID TUMORS

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Background Camidanlumab tesirine (Cami) is an anti-CD25 antibody conjugated to a pyrrolobenzodiazepine dimer cytotoxin designed to deplete CD25+ regulatory T cells (T_{regs}), thereby increasing the CD8+ cytotoxic T-lymphocyte (CTL): T_{reg} intratumoral balance. Here, we report clinical and biomarker data from a phase 1 clinical trial of Cami as monotherapy and in combination with pembrolizumab (NCT03621982).

Methods The primary objective was to characterize the safety and tolerability of monotherapy and combination therapy in patients (pts) aged ≥18 years with select advanced solid tumors who had exhausted standard of care therapy. Secondary and exploratory objectives included evaluation of preliminary antitumor activity, pharmacokinetics, biomarkers, and immunogenicity. Monotherapy and combination dose escalation both utilized a 3+3 design. As monotherapy, pts received Cami every 3 weeks (Q3W) at escalating dose levels. In combination, pts received pembrolizumab 200mg Q3W every cycle and Cami Q3W for 2 out of every 4 cycles (2 cycles with Cami, followed by 2 cycles without) at escalating dose levels.

Results As of 22 December 2022, 44 patients were treated with Cami monotherapy at doses from 20ug/kg to 150ug/kg. No dose limiting toxicities (DLTs) were reported and the maximum tolerated dose (MTD) was not reached. The most common AEs ≥grade 3, regardless of relationship, were anemia (9.1%), abdominal pain, pulmonary embolism, and rash (6.8% each). Stable disease (SD) was observed in 25% of patients. Thirty-four patients were treated with the combination at doses from 30ug/kg to 100ug/kg. Two DLTs were reported: 1 pneumonitis grade 3 and 1 pancreatitis grade 3. The MTD was not established. The most common AEs ≥grade 3, regardless of relationship, were maculo-papular rash (17.6%), anemia (14.7%), hyponatremia, and decreased lymphocyte count (11.8% each). The disease control rate (1 CR + 4 PR + 10 SD) for the combination cohort was 45.5%. All five responses, along with 3 SDs, were observed among the 18 heavily pretreated patients with ovarian cancer (median prior line of therapy=4; ORR 28%, disease control rate 44%). CTL:T_{reg} balance was altered consistent with the expected mechanism of action of Cami. Biomarkers data in circulation and tumor microenvironment will be reported and correlated with efficacy data.

Conclusions Cami is well-tolerated as monotherapy with no major safety signals. The combination of Cami with pembrolizumab is associated with an increase rate of skin and immune-related AEs. The combination shows encouraging results in heavily pre-treated ovarian cancer pts.

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Ethics Approval All trial investigators received approval from their respective institutional review boards or independent ethics committees. The trial was conducted according to Good Clinical Practice guidelines, per the International Conference on Harmonisation. All patients provided written informed consent before participation.

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