## 502 RECOMMENDED PHASE 2 DOSE, PHARMACOKINETICS, PHARMACODYNAMICS, AND PRELIMINARY EFFICACY OF THE IL-15 SUPERAGONIST SO-C101 AS MONOTHERAPY IN PATIENTS WITH ADVANCED/METASTATIC SOLID TUMORS

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**Background** SO-C101 is a superagonist fusion protein of IL-15 and the IL-15 receptor α sushi+ domain. SO-C101 was investigated in a multicenter, open-label, dose escalation study as monotherapy and in combination with pembrolizumab in patients with selected advanced/metastatic tumors (NCT04234113).

**Methods** The SO-C101 monotherapy part of the study followed a classical 3+3 dose escalation design. Study objectives were to determine the maximum tolerated dose (MTD) and the recommended phase 2 dose (RP2D).The evaluation period for dose-limiting toxicities in each dose step was 21 days. The RP2D was defined as MTD or below, also considering pharmacokinetic and pharmacodynamic parameters.The study is ongoing (data cut-off 21 June 2021).

**Results** Thirty patients with a median of 3 (range 1–9) lines of previous systemic therapies were treated at doses 0.25, 0.75, 1.5, 3.0, 6.0., 9.0, 12.0, and 15 µg/kg. At 15 µg/kg, 2 of 3 patients had a dose-limiting toxicity (hyperbilirubinaemia grade [G] 4 and transaminase increase G3). The MTD was reached at 12 µg/kg. This dose was determined as the RP2D, supported by a dose-dependent increase in NK- and CD8+ T cell activation, the latter reaching a plateau at 12 µg/kg. SO-C101 plasma concentration increased dose-proportionally (Tmax was 5.5 hours and T1/2 was 4 hours).The most common adverse events (AEs) were G1 or G2 lymphopenia, local injection site reactions, transaminase increase, flu-like syndrome, and CRS-related symptoms such as fever and chills. Study drug-related AEs >G2 that occurred more than once were lymphopenia and transaminase increase. No treatment-related death was reported.One patient with cutaneous squamous cell carcinoma, who had previously progressed on cemiplimab, showed a partial response at 6.0 µg/kg (duration >4 months, target lesion decrease of 58%). After progression, the patient was put on combination treatment (SO-C101 and pembrolizumab) and again achieved a significant partial response. Two other patients treated with doses below the RP2D had confirmed stable disease for 6 and 15 weeks.At the RP2D, one patient out of 6 discontinued due to progression, while 5 are stable and receiving treatment (range 4–11 weeks).

**Conclusions** The RP2D was defined at 12 µg/kg. SO-C101 administration induced a strong activation of peripheral NK and CD8+ T cells reproducible after each dosing. Related AEs were manageable and resolved quickly. Preliminary clinical efficacy signals including stable disease and partial response were observed in this heavily pretreated patient population. SO-C101 monotherapy has the potential to provide additional clinical benefit to patients with solid tumors.

**Trial Registration** NCT04234113

**Ethics Approval** This study was approved by the FDA (IND 140011) and by the Ethics Boards of participating institutions.

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