484 PRELIMINARY EFFICACY OF THE IL-15 SUPERAGONIST SO-C101 IN COMBINATION WITH PEMBROLIZUMAB IN PATIENTS WITH ADVANCED/METASTATIC SOLID TUMORS

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Background SO-C101 (IL 15/IL-15Rα sushi + domain fusion protein) 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). Synergistic effects of SO-C101 and an anti-programmed cell death protein 1 (PD-1) antibody have been validated in various tumor mouse models inducing a protective memory response.

Methods The combination part of the study follows a classical 3+3 dose escalation design. Study objectives are 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 is 21 days. The RP2D is defined as MTD or a dose below, taking into consideration pharmacokinetic and pharmacodynamic parameters.The study is ongoing (data cut-off 21 June 2021).

Results A total of 12 patients with a median of 2 (range 1–6) lines of previous systemic therapies were treated at SO-C101 dose levels 1.5 µg/kg (3 patients), 3.0 µg/kg (3 patients), and 6.0 µg/kg (6 patients) together with 200 mg of pembrolizumab. One dose-limiting toxicity of grade (G) 3 cytokine release syndrome (CRS) was observed in one patient at 6.0 µg/kg. The MTD has not yet been reached.Of the treated patients, 2 had long-term stable disease (anal squamous cell carcinoma patient at 1.5 µg/kg, duration 25 weeks; gastric carcinoma patient at 3.0 µg/kg, duration 14 weeks) and 3 achieved a partial response (thyroid gland cancer patient at 3.0 µg/kg, target lesion decrease by 36%; skin squamous cell carcinoma patient at 6.0 µg/kg, target lesion decrease by 40%; and melanoma patient at 6.0 µg/kg, target lesion decrease by 58%). The patients with skin squamous cell carcinoma and melanoma had previously progressed on anti-PD-1 therapy, while the patient with thyroid cancer was anti-PD-1 naïve.The most common study drug-related adverse events were lymphopenia, local injection site reactions, transaminase increase, fever, chills as well as CRS-related symptoms (all mainly G1 or G2 and resolved). The only study drug-related adverse event >G2 that occurred in more than one patient was lymphopenia. No treatment-related death was reported.

Conclusions Although the MTD of SO-C101 in combination with pembrolizumab has not been reached yet, clinical efficacy signals were already observed in 5 patients. Available safety data indicate good tolerability. SO-C101 in combination with pembrolizumab has already shown the potential to provide an 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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