**Background** IL-15 is a member of the common γ-chain family of cytokines that shares functional activities with IL-2. SO-C101 is a superagonist fusion protein of IL-15 and the IL-15 receptor α sushii+ domain. SO-C101 stimulates the proliferation and the cytotoxic activity of NK cells and memory CD8+ T cells.

In pre-clinical studies SO-C101 promoted expansion and activation of human, murine and cynomolgus monkey NK and CD8+ T cells. NK and CD8+ T cell activation correlated with potent monotherapy anti-cancer activity of SO-C101 in metastatic and solid tumor models. The combination of an anti-PD-1 or of anti-cancer monoclonal antibodies with SO-C101 augmented the anti-tumor responses in mouse models. First clinical study was initiated in June 2019 to investigate SO-C101 as monotherapy and in combination with pembrolizumab.

**Methods** The phase 1/1b study currently on-going is a multicenter, open-label, dose escalation study for patients with selected advanced/metastatic solid tumors. The study consists of 2 parts: Part A - dose escalation of SO-C101 as monotherapy; Part B - dose escalation of SO-C101 in combination with pembrolizumab. Study objectives are to define the maximum tolerated dose (MTD) and/or recommended phase 2 dose (RP2D) of SO-C101 in both parts.

**Results** As of September 22nd, 19 subjects were treated in part A in 6 escalating dose levels, and 3 subjects were treated in part B, at dose level 1.

SO-C101 was well tolerated. No DLT was observed, the main AEs related to SO-C101 were injection site reactions, fever, chills, flu-like syndrome, all G1- G2, and transient lymphopenia in 5 subjects, Grade 2 to 4, all resolved within few days.

Preliminary PK results showed the PK profile to be dose-proportional, with a Tmax of approx. 5 – 6 hours after administration and T½ approx. 4 hours.

Preliminary PD analysis showed dose dependent NK and CD8+ T cell activation.

A preliminary efficacy signal has been observed in a patient refractory to anti-PD1 therapy, who showed a RECIST PR with initial 20% shrinkage of target lesions at 6 weeks and 49% shrinkage at 12 weeks on CT-scans.

**Conclusions** To date, SO-C101 has been well tolerated, with a manageable toxicity and encouraging signs of clinical activity. The study will proceed to reach a RP2D in both monotherapy and combination with pembrolizumab. Expansion of the study in selected indications is warranted.

**Trial Registration** https://clinicaltrials.gov/ct2/show/NCT04234113?term=sotio&draw=3&rank=12

**Ethics Approval** The NCT04234113 clinical trial was approved by each investigational site health agency and ethical committee.

**Consent** Written informed consent of patients was obtained prior enrollment in the NCT04234113 clinical trial.

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**Abstract 808 Figure 1** T cell subset analysis by cycle and clinical benefit.

Detection of T cell subsets at C1D1, C3D1, and C9D1. (A) CD3+ T cells decrease from C1D1 to C3D1 in patients with no clinical benefit (p=0.009, n=16). CD3+ T cells are significantly higher at C3D1 in patients with clinical benefit (p=0.02, n=16). (B) CD4+ T cells decrease in patients with no clinical benefit from C1D1 to C3D1 (p=0.01, n=16). (C) CD8+ T cells decrease in patients with no clinical benefit from C1D1 to C3D1 (p=0.03, n=16). (D) CD8+ T effector memory cells decrease significantly in patients with no clinical benefit between C1D1 and C3D1 (p=0.02, n=16). (E) CD4+/CXCR3+ cells decrease significantly in patients with no clinical benefit from C1D1 to C3D1 (p=0.02, n=16). (F) CD8+/CXCR3+ cells decrease significantly from C1D1 to C3D1 in patients with no clinical benefit (p=0.02, n=16).