510 SO-C101, A HIGH-AFFINITY IL-15RBG AGONIST, INDUCES SAFE AND POTENT ANTI-TUMOR IMMUNE ACTIVITIES IN PATIENTS WITH SOLID TUMORS AND SUPPORTS FURTHER CLINICAL INVESTIGATIONS

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Background SO-C101 is a high affinity superagonist fusion protein of interleukin (IL)-15 and the IL-15 receptor α (IL-15Rα) sushi<+/sup> domain, representing a promising clinical candidate for the treatment of cancer. SO-C101 specifically stimulates natural killer (NK) cells and memory CD8<+/sup> T cells with no significant expansion and activation of regulatory T cell compartment.

Methods Blood and tumor samples from patients with advanced/metastatic solid tumors included in Phase clinical I study (NCT04234113) were analysed by flow cytometry, immunohistochemistry and NanoString analyses for the activation of immune cells induced by SO-C101 monotherapy or in combination with pembrolizumab.

Results SO-C101 showed a dose-dependent activity in blood of all patients with no clear correlation between the increase of immune cell proliferation and counts in blood and recruitment of immune cells into the tumor tissue. SO-C101 (RLI-15) as a monotherapy or in combination with pembrolizumab increases immune cell infiltration in tumors in clinically responsive patients in Phase clinical I study (NCT04234113) which is accompanied by NK and CD8<+/sup> T cell activation and cytotoxicity, increased proinflammatory chemokines and IFN-gamma signaling genes signatures.

Conclusions All patients showed dose-dependent pharmacodynamic responses in blood, however SO-C101 activity in the tumor microenvironment might be pivotal for the therapeutic success. Favorable safety profile and potent anti-tumor immune activities in patients with solid tumors support further clinical investigations.

Trial Registration NCT04234113

Ethics Approval This study was approved by the FDA (IND 140011) and by the Ethics Boards of participating institutions. The participants provided written informed consent.

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