SO-C101 INDUCES NK CELL CYTOTOXICITY AND PHARMACODYNAMICS AND PHARMACOKINETICS OF J Immunother Cancer of tumor tissue resections was approved by BioNTech SE regulatory authorities for animal welfare in Germany. The use housed in accordance with German federal and state policies SE at its research facilities in Germany, and the mice were All mice studies were performed by BioNTech Ethics Approval (NCT03917381).

Conclusions Combining PD-L1 blockade with conditional 4-1BB co-stimulation using bispecific antibodies induced T-cell activation, expansion, and cytotoxic activity in vitro and potent anti-tumor activity in vivo superior to CPI. DuoBody-PD-L1 x 4-1BB is currently being evaluated in patients with advanced solid tumors in a first-in-human trial (NCT03917381).

Ethics Approval All mice studies were performed by BioNTech SE at its research facilities in Germany, and the mice were housed in accordance with German federal and state policies on animal research. All experiments were approved by the regulatory authorities for animal welfare in Germany. The use of tumor tissue resections was approved by BioNTech SE’s Ethics Board, approval number 837.309.12 (8410-F).

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0561

SO-C101 INDUCES NK CELL CYTOTOXICITY AND POTENTIALS ANTIBODY-DEPENDENT CELL CYTOTOXICITY AND ANTI-TUMOR ACTIVITY

Background SO-C101 is a superagonist fusion protein of interleukin (IL)-15 and the IL-15 receptor α (IL-15Rα) sushii+ domain. SO-C101 effectively stimulates natural killer (NK) cells and memory CD8+ T cells with no significant expansion and activation of regulatory T cells which translates to anti-tumor efficacy in mouse.

Methods In this study, we investigated different administration schedules of SO-C101 in cynomolgus monkeys to assess its pharmacodynamics and pharmacokinetics properties using intravenous (IV) and subcutaneous (SC) routes of administration.

Results Subcutaneous administration of SO-C101 was more effective than IV administration in terms of activating target immune cells which was correlated to the differences in SO-C101 exposure. Repeated administration of SO-C101 over two weeks promoted an increase of absolute lymphocyte counts and of the circulating NK and CD8+ T cell numbers. Moreover, two administrations on consecutive days were optimal and comparable to four daily administrations. We further determined an optimal schedule for a repetitive SO-C101 SC administration to achieve a cycle-dependent stimulation of NK and CD8+ T cells over the course of 10 weeks. These studies allowed to correlate the concentration to response relationship in vitro with the relationship between Cmax following SC administration and the resulting NK and CD8+ T cell activation levels in vivo. These data were used to determine the starting dose and subsequent dose escalation steps of SO-C101 in an ongoing Phase I clinical trial in patients with advanced solid tumors.

Conclusions Since the potency of SO-C101 to activate NK and CD8+ T cells in vitro is equivalent between human and cynomolgous monkeys, these studies informed the dose and schedule selection for the ongoing Phase I clinical study (NCT04234113).

Ethics Approval Pharmacodynamics and pharmacokinetics studies in cynomolgus monkeys were approved by Ethics Board of an appropriate contract research organizations (CROs)

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0563

PHARMACODYNAMICS AND PHARMACOKINETICS OF SO-C101 IN CYNOMOLGUS MONKEYS

1Nada Podzimkova, 1Irena Adkins*, 2Guy de Martynoff, 2David Bechard, 1Radek Spisek, 1Ulrich Moebius. 1Sotio a.s, Prague, Czech Republic; 2Cytune Pharma, Nantes, France

Background SO-C101 is a superagonist fusion protein of interleukin (IL)-15 and the IL-15 receptor α (IL-15Rα) sushii+ domain. SO-C101 effectively stimulates natural killer (NK) cells and memory CD8+ T cells with no significant expansion and activation of regulatory T cells which translates to anti-tumor efficacy in mouse.

Methods In this study, we investigated different administration schedules of SO-C101 in cynomolgus monkeys to assess its pharmacodynamics and pharmacokinetics properties using intravenous (IV) and subcutaneous (SC) routes of administration.

Results Subcutaneous administration of SO-C101 was more effective than IV administration in terms of activating target immune cells which was correlated to the differences in SO-C101 exposure. Repeated administration of SO-C101 over two weeks promoted an increase of absolute lymphocyte counts and of the circulating NK and CD8+ T cell numbers. Moreover, two administrations on consecutive days were optimal and comparable to four daily administrations. We further determined an optimal schedule for a repetitive SO-C101 SC administration to achieve a cycle-dependent stimulation of NK and CD8+ T cells over the course of 10 weeks. These studies allowed to correlate the concentration to response relationship in vitro with the relationship between Cmax following SC administration and the resulting NK and CD8+ T cell activation levels in vivo. These data were used to determine the starting dose and subsequent dose escalation steps of SO-C101 in an ongoing Phase I clinical trial in patients with advanced solid tumors.

Conclusions Since the potency of SO-C101 to activate NK and CD8+ T cells in vitro is equivalent between human and cynomolgous monkeys, these studies informed the dose and schedule selection for the ongoing Phase I clinical study (NCT04234113).

Ethics Approval Pharmacodynamics and pharmacokinetics studies in cynomolgus monkeys were approved by Ethics Board of an appropriate contract research organizations (CROs)

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0563