SB221: A proof-of-concept study to assess the combination of SON-1010 (IL12-F_HAB) and atezolizumab in patients with platinum-resistant ovarian cancer: Trial in Progress

Sant P. Chawla[1], Bo Gao[2], Carolyn Bampton[3], Brett Hamilton[4], John Cini[5], Susan Dexter[5], Richard T. Kenney[5], and Robert M. Wenham[6]: [1]Sarcoma Cancer Center, [2]Blacktown Cancer and Haematology Centre, [3]Ashford Cancer Centre Research, [4]Albury Wodonga Cancer Care, [5]Sonnet BioTherapeutics, [6]Moffitt Cancer Center

Abstract #TPS5629, Poster #496a

Abstract

Background: Recombinant interleukins (rIL) have had limited clinical success due to inefficient tumor targeting and short PK, requiring frequent dosing that leads to aberrant immunostimulation and toxicity. IL-12 potently activates T and NK cells to produce IFNγ and kill tumor cells, yet dosing strategies have failed to provide adequate therapeutic benefit in humans. We developed a novel platform that delivers immunomodulator(s) linked to a fully-human albumin binding (F_HAB®) domain (Cini, Front Immunol 2023). Single-chain native IL-12 genetically linked to the F_HAB provides enhanced tumor targeting and retention through albumin binding to over-expressed FcRn, GP60, and SPARC in the tumor micro-environment (TME), with an improved PK profile, a dose-sparing effect that decreases the toxicity risk, and a broader therapeutic index. Tumor growth inhibition in an immunologically 'cold' B16-F10 mouse melanoma model showed the efficacy of IL12-F_HAB compared with rIL-12, resulting in significant increases in activated NK, NKT, Th1, and cytotoxic CD8 T cells. SON-1010 is being studied clinically as monotherapy (study SB101) in advanced solid tumors and in healthy volunteers (study SB102) (Chawla, AACR 2023). Atezolizumab (Tecentriq®), an anti-PD-L1 immune checkpoint inhibitor (ICI), has shown preliminary clinical activity in Phase 1 studies of patients with platinum-resistant ovarian cancer (PROC) (Liu, Gyn Onc 2019; Moroney, Clin Canc Res 2020). SON-1010 may 'warm up' the TME to improve ICI effectiveness in these immunologically-active tumors that have high levels of SPARC.

Methods: Study SB221 is a Phase 1b/2a multicenter, dose-escalation and proof-of-concept study to assess the safety, tolerability, PK, PD, and efficacy of SON-1010 administered SC, either alone or in combination with a fixed dose of atezolizumab given IV (NCT05756907). The study is designed in Part 1 to rapidly establish the maximum tolerated dose (MTD) of the combination in patients with advanced solid tumors with up to 5 dose-escalation groups and to expand the dataset using patients with PROC to establish the Recommended Phase 2 Dose (RP2D). Once the likelihood of efficacy is shown in a Simon 2-stage design, this will be followed in Part 2 by an assessment in patients with PROC of the potential for improved efficacy of the combination over SON-1010 alone or the standard of care (SOC). The first dose-escalation cohorts have been enrolled and additional sites are being added to help with recruitment of patients with PROC. Combination of SON-1010 with an ICI offers a unique opportunity to use this extended PK version of IL-12 to augment the potential for tumor control in PROC, which represents a significant unmet medical need.

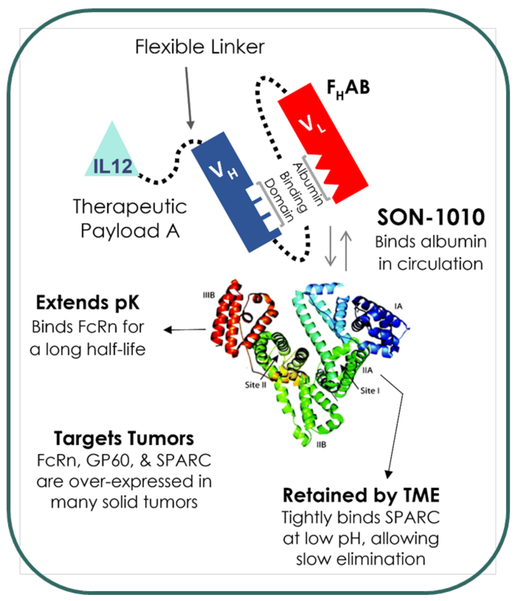
STRUCTURE/FUNCTION

Sonnet's Fully Human Albumin Binding (F_HAB) technology utilizes a single chain antibody fragment (scFv) capable of delivering one or two active drug compounds

- Therapeutic payloads attached via **flexible linker peptides**

Following administration, Sonnet's F_HAB-derived candidates **bind to and "hitch-hike" on endogenous human serum albumin (HSA)** for transport to target tissues

- F_HAB has been designed to **bind, unbind and rebind to albumin** in an on-and-off fashion through a physical bonding mechanism, obviating the need for chemical conjugation



KEY FEATURES

Fully Human Construct
- Low/No immunogenicity
- Single- or Bi-specific design

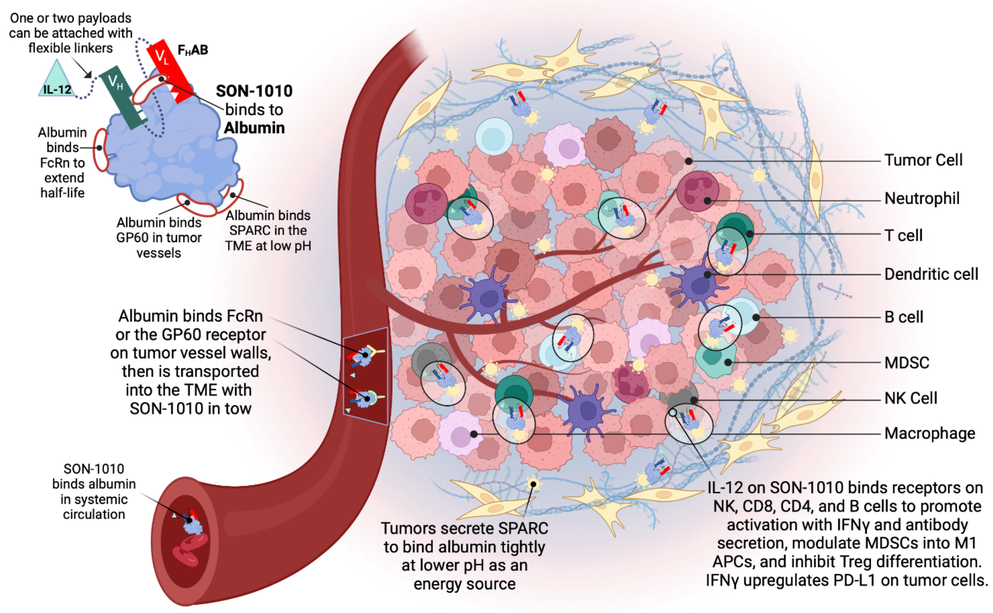
Targeted Delivery
- High efficacy with low side effects
- GP60- and SPARC-driven uptake
- Accumulation in lymphatic nodes

Enhanced pK Characteristics
- Extended dosing intervals
- FcRn binding

Small Size with Linear Flexibility
- Optimized tumor penetration

Mammalian Cell Production (CHO)
- Glycosylated

Modular
- Off-the-shelf system
- Rapid asset development



Portielje, Clin Canc Res (1999) 5:3983; Gokhale, Exp Hematol Oncol (2014) 3:11; Kenney, Front Imm (2024) 15:1362775

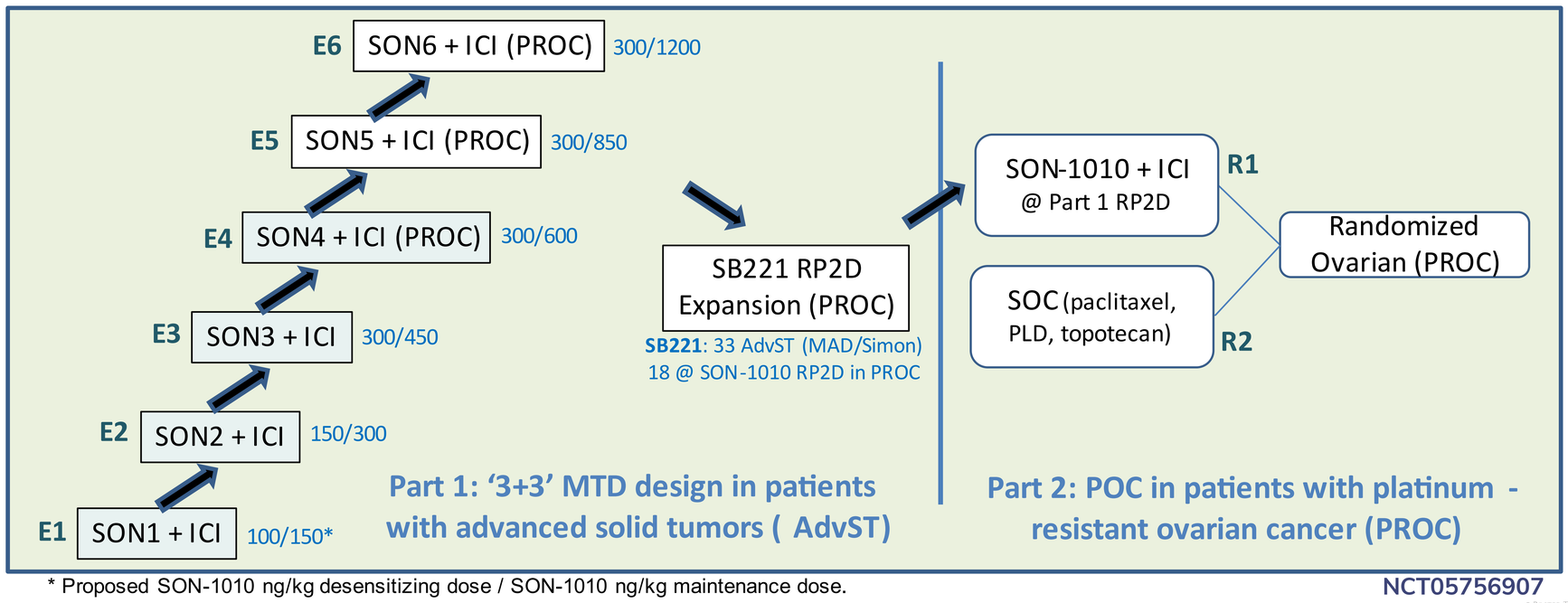
= SON-1010 = SON-1010 activating an immune cell = SPARC = FcRn = GP60 Receptor

Cohorts E1-E3 have been completed without DLTs and E4 is fully enrolled. We are currently enrolling patients with PROC in Cohort E5 at any time after their 1st recurrence following a bevacizumab regimen ± mirvetuxemab. Contact Swati Atole (swati.atole@novotech-cro.com) for trial registration.

Part 1 (N=30-51): Advanced solid tumors → PROC; **Part 2** (N=80, Interim @ 32 events): PROC, defined as ovarian cancer recurrence within 6 months following the last dose of a platinum-containing regimen. Tumor types include epithelial, fallopian tube, or 1° peritoneal carcinoma. Refractory patients, defined as disease that failed to achieve at least a PR to a platinum-containing regimen (i.e., SD or PD), are eligible, provided that outcome was to a 2nd line or later repeated platinum regimen (not 1st line).

SON-1010
Binds albumin in circulation

Atezolizumab
Inhibits PD -L1



* Proposed SON-1010 ng/kg desensitizing dose / SON-1010 ng/kg maintenance dose.

NCT05756907

Scan to download: