Expansion of A Phase 1 Study of SON-1010 (IL12-F_HAB) Adding Trabectedin in Soft Tissue Sarcoma: Trial in Progress

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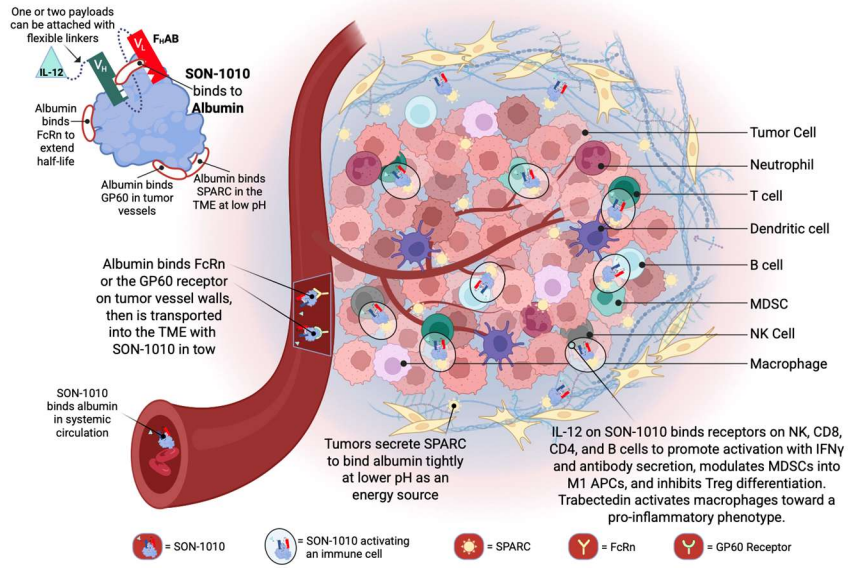
ESMO 2025 Abstract 1598eTiP

Background

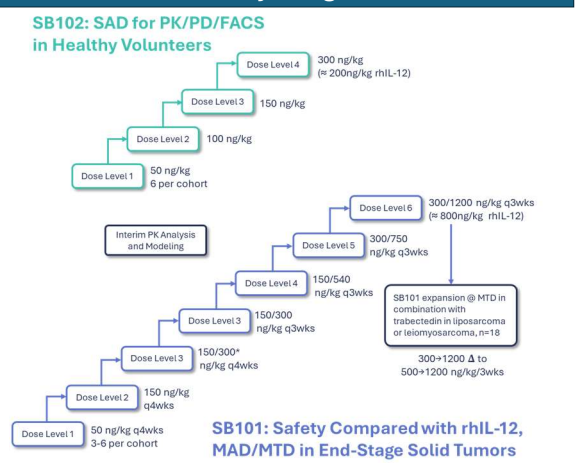
Interleukins have had limited success due to inefficient tumor targeting and short pharmacokinetics (PK), requiring frequent dosing leading to aberrant immunostimulation and toxicity. IL-12 potently activates NK, NKT, Th1, and cytotoxic CD8 T cells to produce IFNγ and efficiently kill tumor cells in mice, yet clinical studies of recombinant IL-12 at the maximum tolerated dose (MTD) of 500 ng/kg have failed to show adequate therapeutic benefit in humans. A novel platform technology was developed that delivers cytokine(s) linked to a fully-human albumin binding (F_HAB®) scFv domain. Single-chain native IL-12 linked to the F_HAB (SON-1010) provides enhanced targeting and retention through albumin binding to over-expressed FcRn, GP60, and SPARC in the tumor microenvironment (TME), with an improved PK profile, a dose-sparing effect that decreases the toxicity risk, and a broader therapeutic index. The safety of SON-1010 along with its PK and PD is being studied clinically as monotherapy (study SB101) in advanced solid tumors and the target MTD of 1200 ng/kg was recently achieved. Trabectedin (Yondelis®) is licensed for patients with metastatic soft tissue sarcoma (STS). While trabectedin is an alkylating drug, it also activates tumor macrophages toward a pro-inflammatory phenotype. SON-1010 may 'warm up' the TME to improve the effectiveness of trabectedin in these immunologically-active tumors.

Trial Design

SB101 is a Phase 1 dose-escalation study that assessed the safety, tolerability, PK, PD, and efficacy of SON-1010 dosed every 3 weeks to establish the MTD (NCT05352750). An expansion cohort adding alternating doses of trabectedin in 18 patients with STS was designed to show added benefit using a Simon 2-stage statistical approach. Enrollment of the expansion cohort is in progress and follow-up is ongoing. The combination of SON-1010 with trabectedin offers a unique opportunity to use this extended half-life version of IL-12 to augment the potential for tumor control in STS, which represents a significant unmet medical need.



Study Design



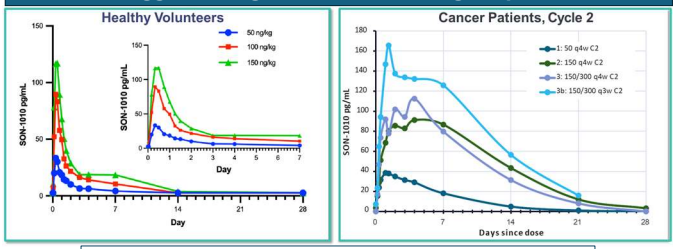
Interim Findings

- Mostly mild adverse events with very few that are more significant
  - No DLTs to date and no dose relationship or change with trabectedin
  - Common AEs (in ≥15%) include fatigue, fever, chills, and myalgia
  - AEs are consistent with published literature for rhIL-12
  - All have been tolerated and are transient in nature
  - AEs are less numerous and less intense after the first dose
- Cytokine results suggest SON-1010 has extended PD with controlled induction of IFNγ, without CRS
- While the formal PFS cannot be established yet, the time to progression averaged 183 days during dose escalation and currently averages 173 days in evaluable patients in the Expansion group with trabectedin.

Safety to Date with Dose Escalation and Trabectedin

SON-1010-Related TEAEs by Gr in ≥2 (≥15% *in bold italics*)	50 ng/kg q4w (N=3)	150 ng/kg q4w (N=3)	150 → 300 ng/kg q4w (N=3)	150 → 300 ng/kg q3w (N=3)	150 → 540 ng/kg q3w (N=3)	300 → 750 ng/kg q3w (N=3)	300 → 1200 ng/kg q3w (N=6)	x00 → 1200 trabectedin q3w (N=18)	x00 → 1200 trabectedin q3w (N=18)	Overall (N=42)
Chills (Gr 1)		1 (33.3)		1 (33.3)			3 (50.0)	6 (33.3)		11 (26.2)
Fatigue (Gr 1)		1 (33.3)		1 (33.3)		1 (33.3)	2 (33.3)	1 (5.6)	2 (11.1)	8 (19.0)
Pyrexia (Gr 1)		1 (33.3)	1 (33.3)		1 (33.3)		1 (16.7)	3 (16.7)		7 (16.7)
Myalgia (Gr 1)	2 (66.7)			1 (33.3)	1 (33.3)		2 (33.3)		1 (5.6)	7 (16.7)
Injection site pain (Gr 1)	1 (33.3)	3 (100.0)								4 (9.5)
Vomiting (Gr 1)									4 (22.2)	4 (9.5)
Headache (Gr 1)		1 (33.3)		1 (33.3)			1 (16.7)			3 (7.1)
Decreased appetite (Gr 1)	1 (33.3)			1 (33.3)		1 (33.3)				3 (7.1)
Nausea (Gr 1)	1 (33.3)					1 (33.3)			2 (11.1)	2 (6.7)
Edema peripheral (Gr 1)	1 (33.3)	1 (33.3)								2 (4.8)
Arthralgia (Gr 1)	1 (33.3)						1 (16.7)			2 (4.8)
Pain in extremity (Gr 1)	1 (33.3)	1 (33.3)								2 (4.8)
Night sweats (Gr 1)		1 (33.3)					1 (16.7)			2 (4.8)
Rash (Gr 1)	1 (33.3)						1 (16.7)			2 (4.8)
Thrombocytopenia (Gr 1)				1 (33.3)				1 (5.6)		2 (4.8)
Fatigue (Gr 2)	3 (100.0)		1 (33.3)			1 (33.3)		3 (16.7)	7 (38.9)	8 (19.0)
Pyrexia (Gr 2)						1 (33.3)		2 (11.1)		3 (7.1)
ALT/AST (Gr 2)		1 (33.3)							1 (5.6)	2 (4.8)
TSH (Gr 2)							1 (33.3)	1 (5.6)		2 (4.8)
Nausea (Gr 2)									2 (11.1)	2 (4.8)
Pruritis (Gr 2)				1 (33.3)			1 (16.7)			2 (4.8)
Thrombocytopenia (Gr 2)								2 (11.1)		2 (4.8)
Anemia (Gr 3)								1 (5.6)	3 (16.7)	4 (9.5)

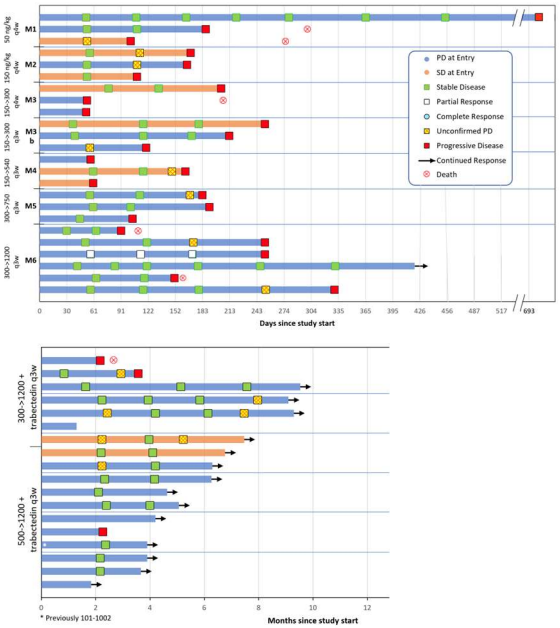
PK suggests Target-Mediated Drug Disposition



- Typical dose-related increases were seen with SC SON-1010, with 1st order elimination kinetics in cancer and 2nd order in HV, suggesting target-mediated drug disposition.
- The preliminary geomean elimination half-life ($T_{½}$) was 113 hours in SB101, compared to 12 hours with rhIL-12.
- C_{max} was 39 to 197 pg/mL with dose escalation and the geomean exposure ($AUC_{0\text{-}inf}$) was 8,620 to 43,600 h*pg/mL.

Kenney, et al, *Front Immunol* (2024) 15:1362775

Interim Responses in SB101



Disclosure Statement
Sonnet BioTherapeutics is sponsoring this trial. Dr. Sant Chawla recently provided funds and will receive stock in Sonnet as part of a Contingency Loan to help defray the costs.