SGN-BB228 is a first-in-class CD228-targeted costimulatory Antibody Anticalin® bispecific delivering potent and conditional 4-1BB costimulation to tumor-specific T cells

Barrett Udeogarai¹, James Mutscher¹, Bryan Grogan¹, Rachida Sham Bel Abir¹, Thomas Jaquín¹, Johannes Urban¹, Markus Zettl¹, Christine Rotheli¹, Shane A. Oelfk¹, Shyra J. Gardai¹, Ryan A. Heiser¹
¹Seagen Inc., Bothell, WA, USA. ²Pfizer Pharmaceuticals GmbH, Hambargern, Germany

Results

CD228 is a tumor-associated antigen with enriched expression in multiple solid tumor types

SGN-BB228 is a first-in-class CD228-targeted costimulatory Antibody Anticalin® fusion bispecific with potent and CD228 conditional 4-1BB costimulatory activity with therapeutic potential in multiple solid tumor types.

Across diverse primary T cell assays, SGN-BB228 displays potent and CD228 conditional costimulation that exceeds the clinical benchmark mAb 20H4.

Altogether, these data support the evaluation of SGN-BB228 in the currently enrolling first-in-human phase 1 clinical study in melanoma and advanced solid tumors. NCT05571839

Conclusions

Disclosures

Background

• SGN-BB228, a first-in-class, investigational, CD228 x 4-1BB McAbalin® bispecific antibody (Anticalin® fusion) was created to overcome the safety and efficacy limitations of systemic anti-4-1BB antibodies.

• SGN-BB228 targets CD228 (melanotransferrin), a GPI-anchored membrane protein with prevalence and high expression across multiple tumor types but limited normal tissue expression.

• SGN-BB228 is designed to provide a potent costimulatory bridge between tumor-reactive cytotoxic T cells and CD228-expressing tumor cells, improving and constraining T cell-mediated cytotoxicity in tumors, and potentially expanding the therapeutic window for 4-1BB agonism.

• CD228 expression is found on multiple solid tumor types but limited normal tissue expression.

• CD228 expression across multiple tumor types but limited normal tissue expression.

Proposed Mechanism of Action

Proposed mechanisms of action in vivo (randomized models): 1. CD228 regulatory T cells (Treg) function is inhibited. 2. Polyclonal signaling is enhanced.

Proposed mechanisms of action in vitro (simplified models): 1. CD228 engagement for costimulation.

4-1BB costimulation across a variety of assays

These data support the evaluation of SGN-BB228 in the currently enrolling first-in-human phase 1 clinical study in melanoma and advanced solid tumors.

SGN-BB228 provides robust costimulation to primary T cells receiving a TCR signal

Conclusions

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Purified T cells cocultured with CD228 expressing tumor cells on anti-CD3 coated plates. CD228 expressing melanoma cell line RPMI-7951 engineered to express CD228. Cocultures were stimulated with CEF viral peptides. CD8 T cell proliferation was measured by flow cytometry. SGN-BB228 drove dose-dependent amplification of CD8 T cell counts compared to parental antibody OMT30 IgG4 FALA and non-targeted IgG4-J10 FALA controls. 4-1BB agonist mAb 20H4.9 failed to provide costimulation in this assay.

SGN-BB228 binds with high affinity to CD228 and 4-1BB

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