Initial clinical and pharmacology results from START-002: A phase 1b/2 clinical investigation of invikafusp alfa (STAR0602), a first-in-class dual T cell agonist, in combination with sacituzumab govitecan in patients with mTNBC or HR+/HER2- mBC

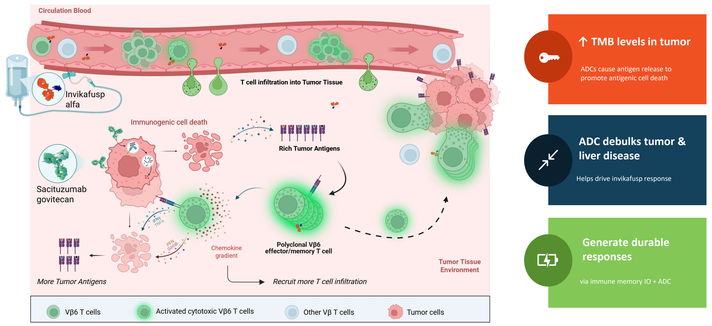
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Background

- Invikafusp alfa ("Invika") is a novel, first-in-class dual T cell agonist that selectively targets subsets of T cells expressing the germline-encoded variable Vβ6 and Vβ10 variant TCRs that are enriched in tumor-infiltrating lymphocytes (TILs).
  - Invika monotherapy generates a potent and selective expansion of CD8+ Vβ6/ Vβ10 T cells.
  - The completed Phase 1 dose escalation study of monotherapy invika (START-001) identified a recommended Phase 2 dose (0.08mg/kg) and demonstrated clinically meaningful single-agent anti-tumor activity in anti-PD(L)-1 resistant tumors, including objective responses in patients with TMB-H triple negative breast cancer (TNBC), colorectal cancer (CRC), non-small cell lung cancer (NSCLC), gastroesophageal junction, gastric, and urothelial cancers.
  - Based on these initial clinical results, the US FDA granted Fast Track Designation for invikafusp alfa in TMB-H CRC.
- Sacituzumab govitecan (SG), an antibody drug conjugate (ADC), is FDA approved for patients with unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) and HR-positive/HER2-negative breast cancer (HR+/HER2- MBC).
  - Preclinical studies indicate ADCs enhance tumor immunogenicity by promoting immunogenic cell death, increased antigen presentation and tumor immune infiltration. These effects are likely mediated by cytotoxic tumor cell death and subsequent release of tumor-associated antigens.
  - Recent clinical results from the ASCENT-04 trial demonstrated improved progression-free survival in previously untreated PD-L1+ mTNBC patients who received the combination of SG and pembrolizumab, thus confirming the clinical potential of combining an ADC with an IO agent in metastatic breast cancer.
- START-002 presented here explores the hypothesis that combining SG's immunomodulatory potential with invikafusp alfa's selective activation and expansion of tumor-reactive Vβ6/Vβ10 T-cells, will enhance anti-tumor responses and result in improved clinical outcomes in breast cancer patients.



↑ TMB levels in tumor
ADCs cause antigen release to promote antigenic cell death

ADC debulks tumor & liver disease
Helps drive invikafusp response

Generate durable responses
via immune memory IO + ADC

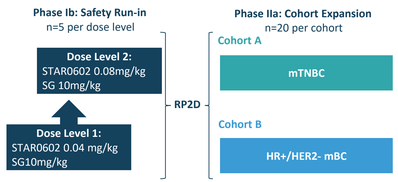
Figure 1. Invikafusp alfa, a bispecific agonist, reinvigorates anti-tumor T cell responses in vivo by selectively activating & expanding Vβ6 memory CD8 T cells in TILs. ADC (SG) increases immunogenic cell death priming for invika to amplify better quality T cell response

START-002

- START-002 is a Phase 1b/2, open label, multi-center study to determine the safety, feasibility, and anti-tumor activity of invikafusp alfa in combination with SG in patients with mTNBC or HR+/HER2- mBC.
- The primary objectives of START-002 are to characterize the safety and tolerability of invikafusp alfa when given together with sacituzumab govitecan and to evaluate preliminary anti-tumor activity of the combination. The primary endpoints are safety and overall response rate per RECIST and iRECIST.
- As of 14Nov2025, 11 patients (10 HR+/HER2- mBC; 3 mTNBC) have been enrolled to the Ph1b Safety Run-in (n=5 pts at Dose Level 1; n=6 pts at Dose Level 2) and 2 patients in the Ph2a Expansion Cohorts of START-002.

ClinicalTrials.gov ID: NCT06827613

Study Schema & Baseline Characteristics



Key Eligibility Criteria
- ECOG 0 or 1
- Measurable disease per RECIST
- Life expectancy ≥12 weeks
- Treated and asymptomatic CNS metastasis allowed

Patient Population
- **3L+ mTNBC:** Progression or recurrence of locally advanced or metastatic TNBC in participants who have received 2 or more prior systemic therapies, at least 1 of them for metastatic disease
- **2L+ HR+/HER2- mBC**: Progression or recurrence of locally advanced or metastatic HR+/HER2- breast cancer in participants who have received prior endocrine based therapy and at least 1 additional systemic therapy in the metastatic setting

- Phase Ib: Two safety run-in cohorts at dose levels of 0.04 mg/kg or 0.08mg/kg of invika in combination with the standard dose of SG (10mg/kg). The RP2D was determined to be 0.08mg/kg invika + 10mg/kg SG.
- Phase IIa: Expansion cohorts for patients with mTNBC or HR+/HER2- mBC. Phase 2 includes a Simon's 2-stage design and will enroll up to 20 participants into each expansion cohort.
- Patients were heavily pretreated (77% pts had ≥4L prior tx) and ADC naïve (12 of 13 pts). 1 patient had prior anti-PDL1 treatment.

Baseline Characteristics		All Patients (n=13)
Age, median (range) - yr		57 (47, 68)
Female sex, n (%)		13 (100%)
Race, n (%)	Asian	1 (8%)
	Black / African American	1 (8%)
	White	10 (77%)
	Unknown	1 (8%)
ECOG, n (%)	0	5 (39%)
	1	8 (62%)
Prior Lines of Therapy, n (%)	2L	1 (8%)
	3L	2 (15%)
	≥4L	10 (77%)
Prior treatment with anti-PD(L)1 n (%)	Yes	1 (8%)
	No	12 (92%)
Prior treatment with ADC, n (%)	Yes	1 (8%)
	No	12 (92%)
Histology, n (%)	TNBC	3 (23%)
	HR+/Her2-	10 (77%)

Safety Profile

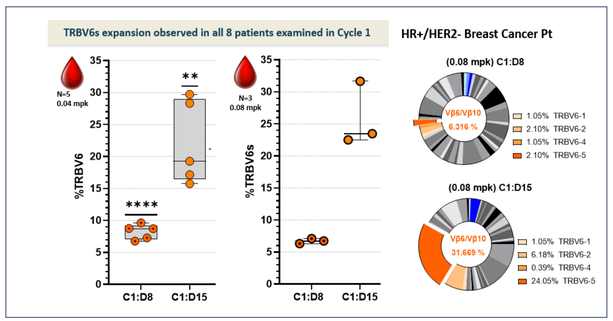
	Most Frequent Treatment-Related Adverse Events (n=13)					
Preferred Term	All Grades	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Cytokine release syndrome	11 (84.6%)	1 (7.7%)	10 (76.9%)	-	-	-
Diarrhea	9 (69.2%)	2 (15.4%)	4 (30.8%)	3 (23.1%)	-	-
Neutrophil count decreased	7 (53.8%)	-	-	5 (38.5%)	2 (15.4%)	-
Fatigue	5 (38.5%)	-	4 (30.8%)	1 (7.7%)	-	-
Nausea	4 (30.8%)	1 (7.7%)	2 (15.4%)	1 (7.7%)	-	-
Alopecia	3 (23.1%)	-	3 (23.1%)	-	-	-
Platelet count decreased	3 (23.1%)	3 (23.1%)	-	-	-	-
Pruritus	3 (23.1%)	1 (7.7%)	1 (7.7%)	1 (7.7%)	-	-
Pyrexia	3 (23.1%)	3 (23.1%)	-	-	-	-
Stomatitis	3 (23.1%)	-	2 (15.4%)	1 (7.7%)	-	-
Tachycardia	3 (23.1%)	3 (23.1%)	-	-	-	-
Vomiting	3 (23.1%)	1 (7.7%)	1 (7.7%)	1 (7.7%)	-	-

The number shown in the table represents the number of patients who experienced a TRAE at an optimal biologic dose of either 0.08mg/kg or 0.12 mg/kg) (highest grade if the same event was reported more than once in a given patient). All data presented is based on information available in the clinical database as of 17Sep2025

Cytokine Release Syndrome graded by ASTCT consensus grading for CRS and neurologic toxicity associated with immune effector cells; all other AEs graded by CTCAE Version 5.0

- Cytokine release syndrome (CRS), diarrhea, and neutropenia were the most frequent treatment related adverse events reported in Phase 1b.
- CRS events associated with invikafusp alfa were primarily low grade, ASTCT grade 1 or 2, and medically manageable following established treatment guidelines.
- Neutropenia and diarrhea are known adverse events associated with SG and were managed using established supportive care measures and published guidelines for prophylaxis and treatment of both toxicities.
- Overall, the combination safety profile of invika + SG is consistent with the known safety profile of each agent. No overlapping toxicities were observed. No ICANS (immune effector cell-associated neurotoxicity syndrome) or irAE events were observed.

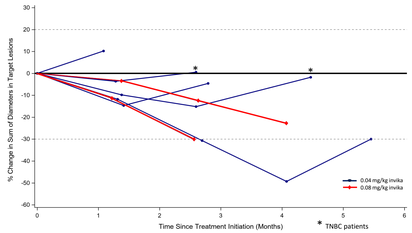
Clinical Pharmacology



- Gene expression analysis demonstrates similar TRBV baseline expression observed in patients treated with invika + SG combination compared with patients treated with invika monotherapy
- Highest levels of TRBV6s were observed at C1D15. The magnitude of TRBV6 increase with invika +SG is consistent with outcomes at the same dose levels observed with invika monotherapy at cycle 1.
- Invikafusp alfa elicited selective expansion in all patients treated with invika + SG. Similar to the adjacent figure, nanostring data from Ph1b patients consistently showed significant increase in TRBV6 population of T cells after cycle 1.

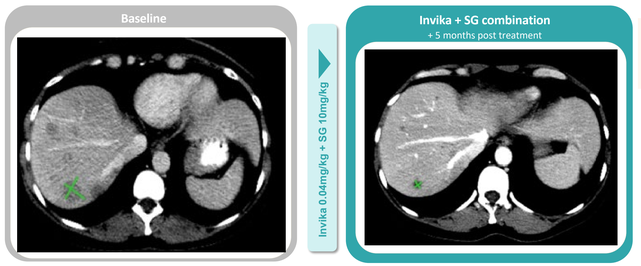
Clinical Efficacy

Figure 2. Ph1b anti-tumor activity of SG + invikafusp alfa



- As of 14-Nov-2025, preliminary efficacy data is available from 7 patients. There has been 1 confirmed response at dose level 1 and 1 unconfirmed response at dose level 2. Four additional patients with RECIST stable disease showed tumor shrinkage. One patient had progressive disease.

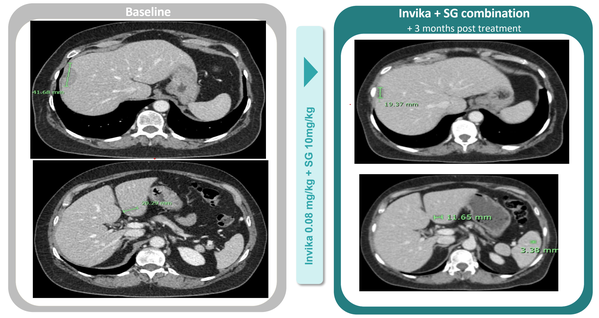
Figure 3. Case Report of Confirmed PR at Dose Level 1



- 57-year-old
- HR+/HER2- mBC
- 4L of prior tx
- liver & bone mets

Confirmed PR (TL -49%)

Figure 4. Case Report Unconfirmed PR at Dose Level 2



- 58-year-old
- HR+/HER2- mBC
- 4L of prior tx
- liver & bone mets

Unconfirmed PR (TL -30.2%)

STARt-002: Key Observations and Next Steps

- Invika in combination with SG is feasible and safe at the doses tested.
- Combination safety profile is consistent with the known safety profile of each individual agent.
- Consistent with its mechanism of action, invikafusp alfa demonstrated unequivocal selective expansion of Vβ6/10 T cells when given with SG in mBC patients.
- Initial clinical anti-tumor activity, including confirmed PR has been observed in patients with previously treated mBC.
- A RP2D has been selected and enrollment to Ph2 expansion cohorts is ongoing to further investigate the clinical activity of this promising novel combination therapy.