PHASE 1 STUDY OF SGN-PDL1V, A NOVEL, INVESTIGATIONAL VEDOTIN ANTIBODY–DRUG CONJUGATE DIRECTED TO PD-L1, IN PATIENTS WITH ADVANCED SOLID TUMORS (SGNPDL1V-001, TRIAL IN PROGRESS)

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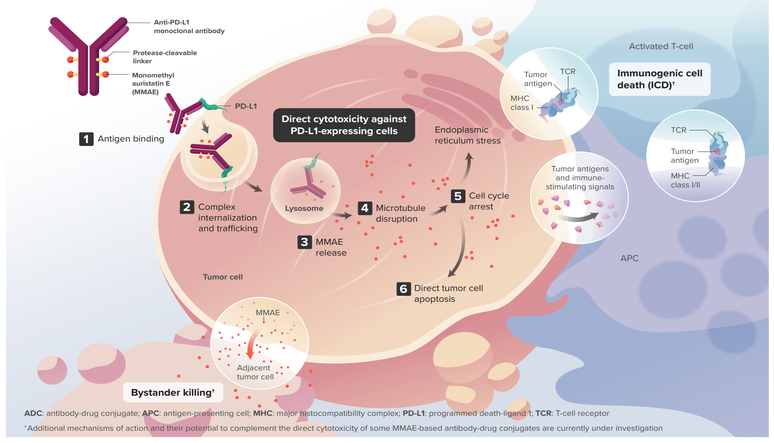
BACKGROUND

- Expression of programmed cell death ligand 1 (PD-L1), a cell-surface protein, is elevated across a broad spectrum of solid tumor types relative to normal tissue, and high expression of PD-L1 is associated with poor prognoses across several solid tumors[1,2]
- PD-L1 is involved in the PD-1/PD-L1 immune checkpoint, which inhibits T-cell activation. Inhibition of the PD-1/PD-L1 signaling axis can play a role in restoring antitumor immunity[1]
- SGN-PDL1V is a novel, investigational antibody-drug conjugate comprised of a PD-L1-directed monoclonal antibody conjugated to monomethyl auristatin E (MMAE) via protease-cleavable linker
- Preclinical studies with SGN-PDL1V demonstrated antitumor activity in PD-L1-expressing tumor xenograft models[3], thus providing rationale for this Phase 1 study
- SGNPDL1V-001 (NCT05208762) is a first-in-human study designed to evaluate the safety, tolerability, pharmacokinetics, and antitumor activity of SGN-PDL1V in patients with advanced solid tumors

SGN-PDL1V PROPOSED MECHANISM OF ACTION



***SGN-PDL1V is an investigational agent, and its safety and efficacy have not been established.**

ELIGIBILITY

Key Inclusion Criteria

- Parts A and B
  - Pts must have one of the following histologically or cytologically-confirmed metastatic or unresectable solid tumor types: NSCLC, HNSCC, or esophageal SCC
  - Pts must have disease that is relapsed or refractory and no appropriate SoC option
- Part A
  - Requires PD-L1 expression ≥1 by TPS or CPS based on historical testing
- Part C
  - Dose expansion: Relapsed or refractory disease or intolerant to SoC therapies:
    - » HNSCC
    - » NSCLC
    - » Esophageal SCC
    - » Ovarian Cancer
    - » Melanoma
- Parts A, B, and C
  - ≥18 years of age, ECOG PS of 0–1, and measurable disease per RECIST v1.1

Key Exclusion Criteria

- Active CNS metastases unless previously treated and can provide evidence of the following:
  - Clinically stable for at least 4 weeks prior to study entry
  - No new or enlarging brain metastases
  - Off corticosteroids prescribed for minimum of 7 days before treatment
- History of other malignancies in the past 3 years or residual disease
- Prior treatment with an anti-PD-L1 agent within past 6 months
- Previous treatment with an MMAE-containing agent
- Pre-existing neuropathy ≥ Grade 2 per NCI CTCAE v5.0
- Leptomeningeal disease

STUDY DESIGN

PHASE 1 • OPEN-LABEL • MULTICENTER

Part A: Dose Escalation
NSCLC 2L+
HNSCC 2L+
Esophageal SCC 2L+
PD-L1 ≥1

→

Part B: Dose and Schedule Optimization*
NSCLC 2L+
HNSCC 2L+
Esophageal SCC 2L+
PD-L1 ≥1

→

Part C: Dose Expansion**
- HNSCC
- NSCLC
- Esophageal SCC
- Ovarian Cancer
- Melanoma

* If neccessary. May examine alternative doses and schedules.
** Signal seeking and Biology cohorts may be evaluated based on data from Parts A and B.

STUDY TREATMENT

- **Part A (dose escalation)** will evaluate SGN-PDL1V at different doses and dose schedules. Alternative dosing schedule(s) may be evaluated in parallel
- **Part B (dose and schedule optimization)** will evaluate the recommended dose and schedule(s) for expansion, from Part A, in different tumor types
- **Part C (dose expansion)** may be activated, including signal seeking and biology cohort(s), after optimal dose and schedule is identified in Parts A or B

OBJECTIVES

Primary Objective	Primary Endpoints
• Evaluate the safety and tolerability	• Incidence, severity, and relatedness of AEs and SAEs • Incidence and severity of laboratory abnormalities
• Identify the MTD	• Incidence of DLTs
• Identify recommended dose and schedule	• Incidence of DLTs, cumulative safety by dose level
Secondary Objectives	**Secondary Endpoints**
• Assess antitumor activity • Assess the PK • Assess immunogenicity	• ORR per RECIST v1.1 by investigator assessment • DOR, PFS by investigator assessment, and OS • Estimate PK parameters (AUC, C_{max}, T_{max}, $t_{1/2}$, C_{trough}) • Incidence of ADAs
Exploratory Objectives	**Exploratory Endpoints**
• Characterize PD • Assess PK/PD relationships	• Exploratory biomarkers of SGN-PDL1V • Correlative analyses of PK and PD exposure

ASSESSMENTS

- Safety assessments will include the monitoring and recording of AEs, concomitant medication, physical examination findings, and laboratory tests
- Determination of antitumor activity will be based on objective response assessments as defined aby RECIST v1.1 and corresponding 95% CIs will be presented where appropriate
- Safety and antitumor activity endpoints will be summarized using the all-treated-subjects analysis set
- DOR, PFS, and OS will be estimated using the Kaplan-Meier method
- Blood samples will be collected for PK and ADA analysis and will be summarized using descriptive statistics

SUMMARY

- SGN-PDL1V is a novel, investigational ADC directed to PD-L1 that is thought to induce antitumor effects through MMAE-directed cytotoxicity, bystander effect, and immunogenic cell death
- Expression of PD-L1, a cell-surface protein, is elevated across several solid tumor types, relative to normal tissue, and high expression of PD-L1 is associated with poor prognoses
- The SGNPDL1V-001 trial is evaluating the safety, tolerability, PK, and antitumor activity of SGN-PDL1V in adults with solid tumors
- Enrollment is ongoing in the United States and planned in EU

Abbreviations

ADA: anti drug antibody; **ADC:** antibody-drug conjugate; **AE:** adverse event; **AUC:** area under the concentration-time curve; **C_{max}:** maximum concentration; **CI:** confidence interval; **CNS:** central nervous system; **CPS:** combined positive score; **C_{trough}:** trough concentration; **DLT:** dose-limiting toxicity; **DOR:** duration of response; **ECOG PS:** Eastern Cooperative Oncology Group performance status; **HNSCC:** head and neck squamous cell carcinoma; **MMAE:** monomethyl auristatin E; **MTD:** maximum tolerated dose; **NCI CTCAE:** National Cancer Institute Common Terminology Criteria for Adverse Events; **NSCLC:** non-small cell lung cancer; **ORR:** objective response rate (CR or PR); **OS:** overall survival; **PD:** pharmacodynamic; **PD-1:** programmed cell death protein 1; **PD-L1:** programmed cell death ligand; **PFS:** progression-free survival; **PK:** pharmacokinetics; **PTS:** patients; **RECIST:** Response Evaluation Criteria in Solid Tumors; **SAE:** serious adverse event; **SCC:** squamous cell carcinoma; **SoC:** standard of care; **$t_{1/2}$:** half-life; **T_{max}:** time to maximum concentration; **TPS:** tumor proportion score

Acknowledgements

The authors thank all our patients and families for their participation in the study and to all research personnel for their support of this trial.
Hanna Thomsen, PhD (employee and stockholder of Seagen Inc.) provided medical writing and editorial support in accordance with Good Publication Practice (GPP3) guidelines.

References

1. O'Malley et al, Mod Pathol. 2019; 32:929-942
2. Cha et al, Mol Cell. 2019; 76(3):359-370
3. Kwan et al, J Imm Can. 2021; 9(Suppl 2):A818

American Society of Clinical Oncology Annual Meeting; June 3−7, 2022; Abstract No. TPS3154