PHASE 1b/2 STUDY OF LADIRATUZUMAB VEDOTIN (LV) IN COMBINATION WITH PEMBROLIZUMAB FOR FIRST-LINE TREATMENT OF TRIPLE-NEGATIVE BREAST CANCER (SGNLVA-002, TRIAL IN PROGRESS)

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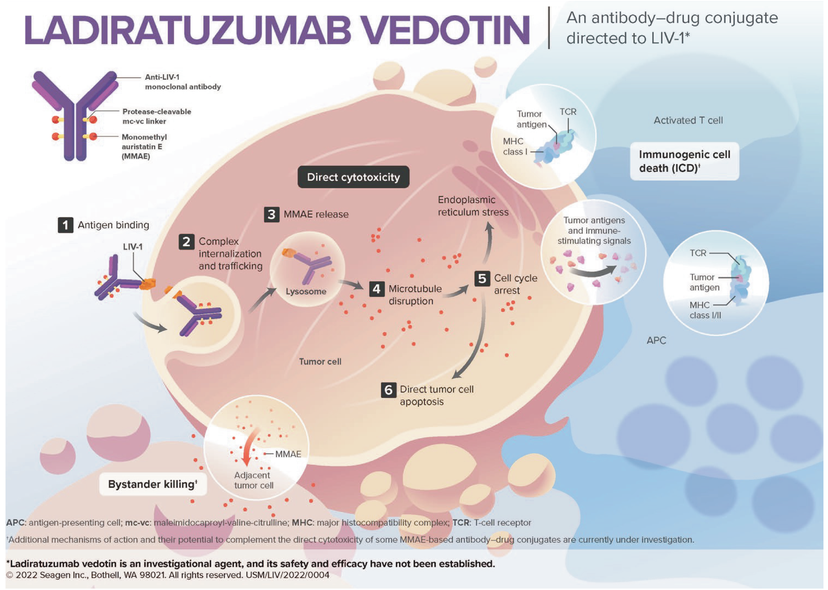
BACKGROUND

- Triple-negative breast cancer (TNBC) is a highly aggressive sub-type of breast cancer associated with poor outcomes and a high mortality rate[1]
  - Programmed death ligand-1 (PD-L1) low/negative TNBC represents an unmet medical need
- LIV-1 is a transmembrane protein involved in the signaling pathway leading to epithelial-mesenchymal transition and its expression has been linked with malignant progression to metastasis in breast cancer[2–4]
- LIV-1 is expressed in ≥90% of all clinical subtypes of metastatic breast cancer tumors and has low expression in normal tissues[5,6]
- LV is an investigational antibody–drug conjugate directed to LIV-1 via a humanized immunoglobulin G1 monoclonal antibody conjugated to monomethyl auristatin E (MMAE) by a protease-cleavable linker[5]
- LIV-1–mediated delivery of MMAE causes microtubule disruption, thereby inducing cell cycle arrest and apoptosis[7]
- Preliminary results showed LV delivered once every 3 weeks + pembrolizumab was tolerable with encouraging antitumor activity in patients with metastatic TNBC (mTNBC)[6]
- Interim results of weekly LV monotherapy at doses up to 1.5 mg/kg showed that LV was clinically active and generally well tolerated[8]
- Based on pharmacokinetic and pharmacodynamic modeling and simulation analysis, an intermittent LV + pembrolizumab dosing regimen is being evaluated to further enhance efficacy and improve the tolerability profile

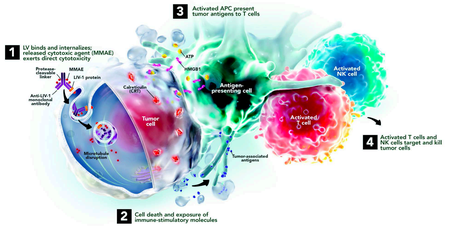
PROPOSED MECHANISMS OF ACTION OF LV



***Ladiratuzumab vedotin is an investigational agent, and its safety and efficacy have not been established.**

RATIONALE FOR COMBINING LV WITH PEMBROLIZUMAB

- LV and pembrolizumab act through distinct and complementary mechanisms
- LV-induced immunogenic cell death (ICD) elicits an inflammatory response, leading to enhanced antitumor immunity
  - Increased antigen presentation
  - Increased tumor immune cell infiltration[7]
- LV-induced ICD creates a microenvironment favorable for enhanced pembrolizumab activity



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ELIGIBILITY: PART D

Key Inclusion Criteria

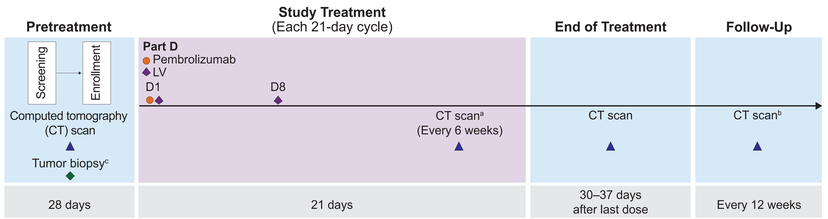
- ≥18 years of age
- Unresectable locally advanced (LA) or metastatic, histologically documented TNBC (absence of human epidermal growth factor receptor 2 overexpression or amplification, estrogen receptor, and progesterone receptor expression)
- LIV-1 expression is not an eligibility requirement
- Tumor tissue PD-L1 combined positive score <10 using the PD-L1 immunohistochemistry 22C3 clone
- No prior cytotoxic therapy for the treatment of unresectable LA or mTNBC
- At least 6 months since prior neoadjuvant and/or adjuvant treatment with curative intent and recurrence
- Measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1
- An Eastern Cooperative Oncology Group performance status (ECOG PS) score of 0 or 1
- Adequate hematologic, kidney, and liver function

Key Exclusion Criteria

- Prior immune-oncology therapy
- Pre-existing neuropathy of at least Grade 2
- Active central nervous system metastases
- Active autoimmune disease requiring systemic treatment within the past 2 years

STUDY DESIGN: PART D

- SGNLVA-002 (NCT03310957) is an ongoing global single-arm, open-label, phase 1b/2 study of LV + pembrolizumab as first-line therapy for patients with unresectable LA or mTNBC
- In Part D, approximately 40 patients will receive LV 1.5 mg/kg administered on Day 1 and Day 8 (off Day 15) of every 21-day cycle in combination with pembrolizumab administered on Day 1 of every cycle



[a]Response assessments to be performed every 6 weeks (±3 days) for the first 12 months and every 12 weeks (±7 days) thereafter, regardless of dose delays. For first objective response (complete or partial response), a scan will be performed at least 4 weeks after first documentation of response. [b]Patients who discontinue study treatment in the absence of disease progression will continue to be evaluated for response every 6 weeks for the first 12 months on study and every 12 weeks thereafter until progression or initiation of a new anticancer treatment. Patients will be followed for overall survival every 12 weeks. [c]Archival or newly obtained core or excisional tumor biopsy.

OBJECTIVES

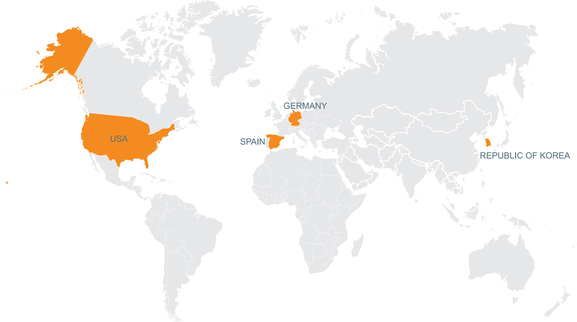
Primary Objective	Endpoints
• To evaluate the safety and tolerability of LV + pembrolizumab	• Type, incidence, severity, seriousness, and relatedness of adverse events (AEs) and laboratory abnormalities
• To evaluate the antitumor activity of LV + pembrolizumab	• Confirmed objective response rate (ORR) as determined by the investigator according to RECIST v1.1
Secondary Objectives	**Endpoints**
• To evaluate the long-term outcomes and duration of response of LV + pembrolizumab	• Duration of response (DOR), disease control rate (DCR), and progression-free survival (PFS) as determined by RECIST v1.1 • Overall survival
Exploratory Objectives	**Endpoints**
• To evaluate antitumor activity according to Immune RECIST (iRECIST)	• ORR, DOR, DCR, and PFS as determined by iRECIST
• To assess PD-L1 and LIV-1 expression-response relationship	• PD-L1 and LIV-1 expression-response relationship following treatment with LV and pembrolizumab

ASSESSMENTS

- Efficacy assessments: Antitumor activity will be assessed by radiographic tumor imaging at protocol-specified time points
- Safety assessments: Surveillance and recording of AEs, physical examination findings, vital signs, electrocardiogram, concomitant medications, and laboratory tests
- Statistical analysis: Safety and efficacy endpoints will be summarized with descriptive statistics

SUMMARY

- Part D of the SGNLVA-002 study will assess the safety and antitumor activity of LV in combination with pembrolizumab for patients with LA or mTNBC who are PD-L1 low or negative
- Global enrollment is ongoing in the US, EU, and Asia



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