Background

**SL-172154** (Fc-CD40L) is a humanized, bi-functional fusion protein consisting of CD40L (ligand)-truncated CD40L (ligand) linked to CD44 via a 6-amino-acid linker (Cys-Leu-Val-Leu-Pro-Lys) that bridges innate and adaptive immunity.

**Phase 1** dose escalation study of SL-172154 (SIRPα-Fc-CD40L) in platinum-resistant ovarian cancer was to establish the recommended phase 2 dose (RP2D).

**Methods**

**Eligibility criteria**

- **Histologically confirmed, unresectable, locally advanced or metastatic ovarian cancer:** primary peritoneal or fallopian tube cancer.
- **Relying on existing therapy:** and available for further platinum therapy.
- **Age:** 18 years or older.
- **ECOG performance status:** 0 or 1.
- **Measurable disease:** per RECIST v.1.

**Key exclusion criteria**

- **Histologically confirmed, unresectable, locally advanced or metastatic ovarian cancer:** primary peritoneal or fallopian tube cancer.
- **Relying on existing therapy:** and available for further platinum therapy.
- **Age:** 18 years or older.
- **ECOG performance status:** 0 or 1.
- **Measurable disease:** per RECIST v.1.

**Key objective**

- **Maximum tolerated dose (MTD):** as defined by progressive or during within 1 month of up-tick platinum therapy.
- **Primary treatment:** or anti-CD40 or anti-CD40L targeting agent or a CD40 agonist.
- **Documented history:** of autoimmune disease or active psoriasis.

**Key exclusion criteria**

- **MTD:** as defined by progressive or during within 1 month of up-tick platinum therapy.
- **Primary treatment:** or anti-CD40 or anti-CD40L targeting agent or a CD40 agonist.
- **Documented history:** of autoimmune disease or active psoriasis.

**Results**

**Table 1: Study Population and Tumor Characteristics**

**Table 2: Drug-related AE (%):**

**Table 3: AEs by System Organ Class:**

**Table 4: Pharmacokinetic parameters:**

**Table 5: CD8+ Effector T Cells (%):**

**Table 6: Maximal IL-12 Stimulation:**

**Table 7: Fold Change over Pretreatment:**

**Table 8: Safety:**

**Results**

- **CD3+CD8+ GrB+ T cells:** rapidly marginated from the bloodstream and showed a dose-response relationship.
- **Increased egress:** from the bloodstream was observed at 3.0 mg/kg dose and target-mediated drug disposition via receptor inhibition was readily manageable.
- **Infusion-related reactions:** occurred either during the infusion or within 2 hrs after the end of infusion, except one event.
- **Severity and frequency:** of infusion-related reactions were dose-dependent and correlated with rate of infusion.
- **No fatal AEs:** were reported.
- **G3/4 drug-related AEs:** included AST increased (G3), lymphopenia (G4), and all were fully resolved with no dose adjustments.
- **Percent change from predose:** in CD47 saturation on CD4 T cells was greater in subjects in the high dose group compared to those in low dose group.
- **IL-12 stimulation:** in the tumor nest and tumor stroma was increased in subjects in the high dose group compared to those in low dose group.
- **Immunogenicity:** was evaluated by evaluating tumor composition, and was increased in subjects in the high dose group compared to those in low dose group.

**Conclusions**

- **SL-172154:** was overall well-tolerated in patients with heavily pretreated platinum-resistant ovarian cancer.
- **Best response:** among 27 efficacy evaluable subjects with post-baseline scans from Stable Disease (SD) in 13 (56%) subjects (median duration: 39 days to 252 days).
- **Infusion-related reactions:** occurred either during the infusion or within 2 hrs after the end of infusion, except one event.
- **Severity and frequency:** of infusion-related reactions were dose-dependent and correlated with rate of infusion.
- **No fatal AEs:** were reported.
- **G3/4 drug-related AEs:** included AST increased (G3), lymphopenia (G4), and all were fully resolved with no dose adjustments.
- **Percent change from predose:** in CD47 saturation on CD4 T cells was greater in subjects in the high dose group compared to those in low dose group.
- **IL-12 stimulation:** in the tumor nest and tumor stroma was increased in subjects in the high dose group compared to those in low dose group.
- **Immunogenicity:** was evaluated by evaluating tumor composition, and was increased in subjects in the high dose group compared to those in low dose group.

**Acknowledgments**

- **We extend our appreciation:** to study participants and their families.
- **This study:** is funded by Shattuck Labs, Inc. Austin, TX and Durham, NC, USA.
- **Clinical trial registration:** was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice (GCP) guidelines.

**References**