Abstract Number

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STRO-002-GM2: A Phase 1 Open-Label, Safety, Pharmacokinetic and Preliminary Efficacy Study of STRO-002, an Anti-Folate Receptor Alpha Antibody Drug Conjugate, in Combination with Bevacizumab in Patients With Advanced Epithelial Ovarian Cancer (Including Fallopian Tube or Primary Peritoneal Cancers)

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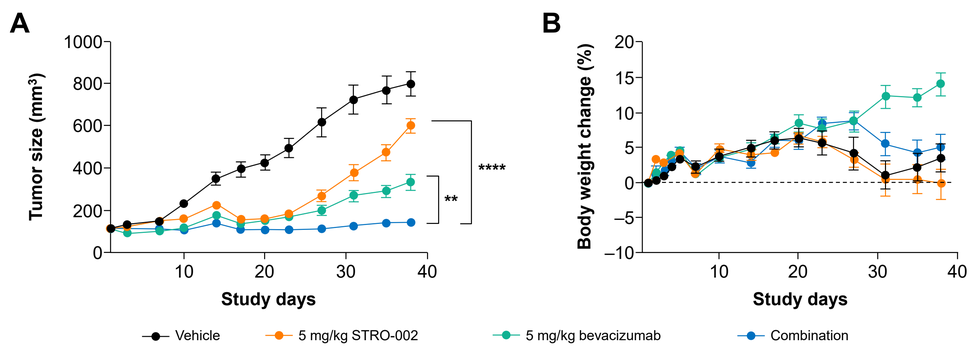
BACKGROUND

- Folate receptor alpha (FolRα) is a cell-surface glycoprotein overexpressed in several cancer types, including epithelial ovarian cancer (EOC) and endometrial adenocarcinoma[1,2]
- STRO-002 is a novel FolRα-targeting antibody drug conjugate (ADC) generated using cell-free antibody production and site-specific conjugation technology, which produces a well-defined ADC drug product with a drug-antibody ratio of 4
- STRO-002 has demonstrated preliminary single-agent activity in platinum-resistant ovarian cancer in a phase 1 dose-escalation study. At the most recent data cutoff in April 2021[3]
  - Ten of 31 evaluable patients demonstrated objective responses (1 complete response [CR], 4 confirmed partial responses [PRs], and 5 unconfirmed PRs)
  - Disease control rates (DCRs) were 61% (≥16 weeks) and 55% (24 weeks)
  - Median progression-free survival (PFS) was 7.2 months
  - Treatment was generally well tolerated
- STRO-002 combined with bevacizumab, a humanized monoclonal antibody against vascular endothelial growth factor (VEGF), demonstrates additive antitumor activity vs monotherapy in *in vivo* ovarian cancer tumor models **(Figure 1)**[4]

Figure 1. STRO-002 in combination with VEGF blockade exhibits added benefit compared with monotherapy in OV-90 tumors[4]



(A) Co-administration of STRO-002 and bevacizumab (anti-VEGF), both administered once, significantly improved human tumor growth inhibition (96% TGI) on day 38 compared with STRO-002 (20% TGI) or bevacizumab (68% TGI) alone. (B) Percentage body weight change relative to animal weight at the start of the study shows that all treatments were well tolerated. Mean ±SEM, statistical analysis on tumor size at indicated days was performed in Prism using one-way ANOVA with Dunnett's or Tukey's multiple comparison test, unless otherwise indicated: p<0.05 was considered significant; ****, p<0.0001; **, p<0.01.
SEM, standard error of mean; TGI, tumor growth inhibition; VEGF, vascular endothelial growth factor.

- The combination of a FolRα-targeting ADC (mirvetuximab) with bevacizumab has demonstrated clinical activity in FolRα-expressing, platinum-resistant ovarian cancer, with higher clinical responses compared with monotherapy in a similar population[5]
  - In patients with high FolRα expression (n=33), the confirmed overall response rate (ORR) was 64%, the median duration of response (DOR) was 11.8 months, and the median PFS was 10.6 months
  - Treatment had a favorable tolerability profile

METHODS

- STRO-002-GM2 is a first-in-human, phase 1, open-label, multicenter, dose-escalation study of STRO-002 given in combination with bevacizumab in patients with advanced EOC who have progressed on standard therapy
- The study will establish the recommended phase 2 dose (RP2D) and assess safety and preliminary efficacy of the STRO-002/bevacizumab combination

Part 1: Dose-escalation phase (Figure 2, Tables 1 and 2)

- Standard 3+3 dose-escalation design with a 21-day dose-limiting toxicity (DLT) assessment period
- Bevacizumab will be administered at the labeled dose of 15 mg/kg, given with STRO-002 starting at a dose of 3.5 mg/kg, both administered intravenously every 3 weeks
- **Aim:** determine the STRO-002 RP2D in combination with bevacizumab

REFERENCES

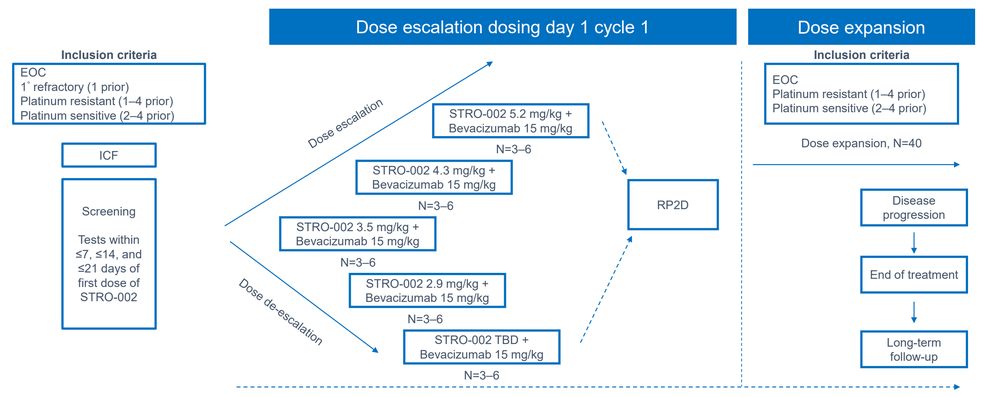
1. Kalli KR et al. *Gynecol Oncol.* 2008;108:619-626.
2. O'Shannessy DJ et al. *Int J Gynecol Pathol.* 2013;32:258-268.
3. Naumann RW et al. Presented at ASCO 2021 (abstract 5550).
4. Abrahams CL et al. Presented at AACR 2022 (abstract 5591).
5. O'Malley DM et al. Presented at ASCO 2021 (abstract 5504).

METHODS (continued)

Part 2: Dose-expansion phase (Figure 2, Tables 1 and 2)

- Dose-expansion phase will enroll approximately 40 patients treated with the RP2D

Figure 2. Study design



Additional intermediate dose level cohorts may be added for RP2D optimization. Once a cohort is cleared per dose escalation rules, up to 10 additional subjects may be enrolled and treated at that cleared dose level to obtain additional safety and efficacy data for RP2D determination and ungating of the expansion stage.
ICF, informed consent form signed; PD, progressive disease; TBD, to be determined.

Table 1. Eligibility

Key inclusion criteria	Key exclusion criteria
High-grade EOC, fallopian tube, or primary peritoneal cancer	Contraindications to bevacizumab treatment
At least 1 radiographically measurable (target) lesion per RECIST v1.1	Prior treatment with a FolRα-targeting ADC
Tumor tissue is required from all patients (archival or fresh biopsy for dose escalation and both for dose expansion)	
≤4 prior treatment regimens	Prior treatment with ADCs containing tubulin inhibitors
Adequate bone marrow, renal, and liver function	

RECIST, Response Evaluation Criteria in Solid Tumors.

Table 2. Objectives and endpoints

Primary objectives	Primary endpoints
Part 1 Dose-escalation phase: Evaluate safety and tolerability of STRO-002/bevacizumab; determine RP2D	AEs, DLTs, clinical laboratory abnormalities, RP2D
Part 2 Dose-expansion phase: Further evaluate toxicity and tolerability of STRO-002/bevacizumab; evaluate tumor response (ORR)	AEs; clinical laboratory abnormalities; ORR defined as CR or PR per RECIST v1.1, as determined by investigator
Secondary objectives	**Secondary endpoints**
Part 1 Dose-escalation phase: Characterize PK and immunogenicity of STRO-002/bevacizumab	PK; ADAs
Part 2 Dose-expansion phase: Evaluate time-to-event endpoints and CA-125 endpoints; further evaluate PK	DOR, DCR, and PFS per RECIST v.1.1 as determined by investigator; CA-125 response and progression per GCIG criteria; PK
Exploratory endpoints	
Part 1 Dose-escalation phase: Preliminary assessment of antitumor activity per RECIST v1.1 (ORR, PFS, DOR, DCR); correlate PK with clinical activity; explore whether biomarkers are predictive of clinical response; toxicity; treatment resistance	
Part 2 Dose-expansion phase: correlate PK with clinical activity; explore whether biomarkers are predictive of clinical response; toxicity; treatment resistance; OS at 12 months	

ADA, antidrug antibody; AE, adverse event; CA-125, cancer antigen-125; GCIG, Gynecologic Cancer Intergroup; OS, overall survival; PK, pharmacokinetic.

- No formal statistical hypothesis testing will be conducted in this study

SUMMARY OF TRIAL AND RATIONALE

- STRO-002 is an investigational FolRα-targeted ADC in development for FolRα-expressing tumors, including ovarian and endometrial cancers
- Based on preliminary clinical data for single-agent STRO-002 and pre-clinical activity of bevacizumab plus STRO-002 in platinum-resistant ovarian cancer, we hypothesize that the combination of STRO-002 plus bevacizumab will provide additional clinical benefit in this patient population
- The primary objective of the STRO-002-GM2 study is to identify the RP2D of the STRO-002/bevacizumab combination and assess the safety of the combination. Secondary and exploratory objectives include PK and preliminary anti-tumor activity
- Enrollment began in March 2022 in the United States; as of May 2022, the study was in the dose escalation phase
- The STRO-002-GM2 study is registered with ClinicalTrials.gov (NCT05200364)

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