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Phase 1 Dose-Escalation Study of STRO-002, an Anti–Folate-Receptor Alpha Antibody Drug Conjugate, in Patients With Advanced, Progressive, Platinum-Resistant/-Refractory Epithelial Ovarian Cancer

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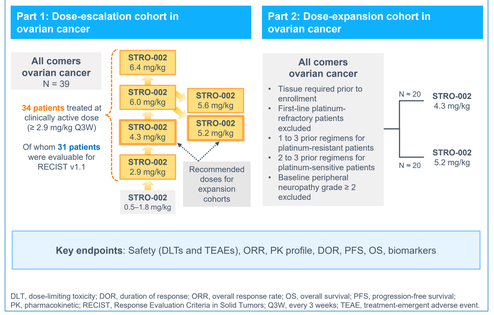
INTRODUCTION

- Folate-receptor alpha (FRα) is a cell surface glycoprotein overexpressed in ovarian cancer and endometrial adenocarcinoma[1,2]
- STRO-002 is a novel FRα-targeting antibody drug conjugate (ADC) with a precise drug-antibody ratio of 4 using site-specific conjugation technology circumventing limitations of current ADCs[3,4]
  - The potential dual mechanism includes
    - A potent tubulin-targeting cytotoxin containing 3-aminophenyl hemiasterlin warhead SC209 that is a weak substrate for P-glycoprotein
    - Immunogenic response upon cell death
- STRO-002-GM1 (NCT03748186) is an ongoing phase 1, open-label study in patients with advanced platinum-resistant or -refractory epithelial ovarian cancer (EOC)

METHODS

- Patients received intravenous STRO-002 on day 1 of each 21-day cycle until disease progression
  - Ocular exams were performed at baseline and every other cycle
  - Prophylactic corticosteroid eye drops were not administered
  - FRα expression was not required for eligibility
  - Retrospective analysis of FRα expression in archival tumor tissue is ongoing
- Results from the dose-escalation cohort are reported here; evaluation of the dose-expansion cohort is ongoing (**Figure 1**)

Figure 1. STRO-002-GM1 study design



DLT, dose-limiting toxicity; DOR, duration of response; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetic; RECIST, Response Evaluation Criteria in Solid Tumors; Q3W, every 3 weeks; TEAE, treatment-emergent adverse event.

RESULTS

- A total of 39 patients were enrolled, and data cutoff was April 23, 2021
- Patients had a median age of 61 years, with median time since diagnosis of 3.9 years and a median of 6 prior lines of therapy (**Table 1**)
- Patients were treated with 9 dose levels; 34 patients were treated at clinically active doses of ≥ 2.9 mg/kg

Table 1. Baseline characteristics

Baseline characteristic	All patients (N = 39)
Age, median (range), years	61 (48–79)
Time since diagnosis, median (range), years	3.9 (0.7–17.0)
No. of prior lines of therapy, median (range)	6 (1–11)
Previous therapies, n (%)	
Platinum	39 (100)
≥ 3 prior platinum regimens	18 (46)
Taxanes	38 (97)
Bevacizumab	32 (82)
Poly (ADP-ribose) polymerase inhibitors	23 (59)
Checkpoint inhibitors	8 (21)
Experimental therapy	14 (36)

ADP, adenosine diphosphate.

- Most TEAEs (86%) were grade 1–2 (**Table 2**)
  - No ocular toxicity signal was observed
  - The most frequent grade 3–4 adverse event was neutropenia (64%, which included neutropenia, febrile neutropenia, and neutrophil count decreased)
- DLTs were observed in 1 patient each at 6 mg/kg (grade 2 neuropathy/ grade 3 arthralgia) and at 6.4 mg/kg (grade 3 bone pain)
- Two grade 5 events were reported, both unrelated to study drug by investigator assessment (1 death not otherwise specified, 1 acute gastrointestinal bleed)

Table 2. Most frequent TEAEs > 25% by grade

All safety-evaluable patients, n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Overall (N = 39)
Fatigue	7 (18)	19 (49)	4 (10)	0	30 (77)
Nausea	15 (39)	11 (28)	0	0	26 (67)
Constipation	12 (31)	13 (33)	0	0	25 (64)
Neutropenia[a]	0	0	8 (21)	17 (44)	25 (64)
Decreased appetite	10 (26)	10 (26)	0	0	20 (51)
Arthralgia	7 (18)	7 (18)	5 (13)	0	19 (49)
Neuropathy[b]	3 (8)	13 (33)	3 (8)	0	19 (49)
Abdominal pain	7 (18)	6 (15)	3 (8)	0	16 (41)
Vomiting	8 (21)	7 (18)	0	0	15 (39)
AST increased	10 (26)	3 (8)	2 (5)	0	15 (39)
Diarrhea	8 (21)	3 (8)	1 (3)	0	12 (31)
Dizziness	9 (23)	3 (8)	0	0	12 (31)
Dry eye	4 (10)	8 (21)	0	0	12 (31)
Anemia	3 (8)	6 (15)	2 (5)	0	11 (28)
Pyrexia	8 (21)	3 (8)	0	0	11 (28)
Headache	7 (18)	3 (8)	0	0	10 (26)
Insomnia	6 (15)	4 (10)	0	0	10 (26)

[a]Neutropenia included the following preferred terms: neutropenia, febrile neutropenia, and neutrophil count decreased. [b]Neuropathy included the following preferred terms: neuropathy peripheral and peripheral sensory neuropathy. AST, aspartate aminotransferase.

KEY FINDINGS

In this phase 1 dose-escalation study, the novel FRα-targeting ADC STRO-002 exhibited a generally well-tolerated safety profile and clinical efficacy as demonstrated by objective responses (1 CR, 4 PRs, and 5 PRus), disease control rate of 61% and 55% at ≥ 16 and 24 weeks, respectively, and median PFS of 7.2 months in heavily pretreated patients with progressive EOC

CONCLUSIONS

- STRO-002 is a novel FRα-targeting ADC that showed a preliminary clinical efficacy signal at multiple doses (≥ 2.9 mg/kg Q3W) in patients with heavily pretreated relapsed/refractory EOC
- Dose reductions were not associated with loss of antitumor activity
- STRO-002 treatment was well tolerated, including in patients with long-term responses (≥ 74 weeks); the majority of TEAEs (86%) were grade 1 or 2
- Antitumor activity was observed across a broad range of FRα expression levels based on PS2+ scoring and H-score
- During the dose-expansion part of the STRO-002-GM-1 study, patients with less heavily pretreated ovarian cancer will be enrolled
- Preliminary data from the dose-expansion cohort is expected later in 2021

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. Li X et al. *Cancer Res*. 2018;78(13 suppl):abstract 1782.
4. Zimmerman ES et al. *Bioconjug Chem*. 2014;255:351-361.

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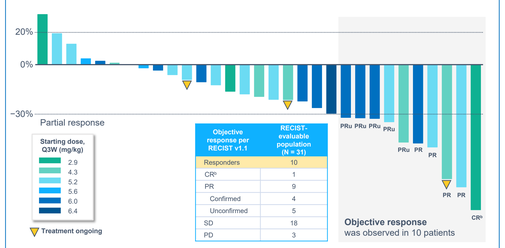
RESULTS (continued)

- 31 of 34 patients were evaluable for RECIST v1.1 response
  - 10 of 31 patients had objective responses: 1 complete response (CR), 4 confirmed partial response (PR), and 5 unconfirmed PR (PRu; **Figure 2**)

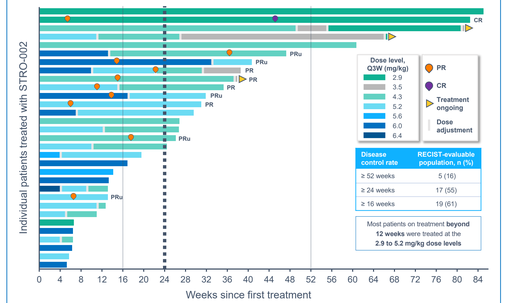
Figure 2. Maximum change[a] in tumor target lesions in RECIST-evaluable patients treated with STRO-002 ≥ 2.9 mg/kg Q3W (N = 31)



[a]Maximum percentage change from baseline in sum of longest diameter in evaluable patients treated with STRO-002 at ≥ 2.9 mg/kg Q3W (N = 31). [b]CR in patient treated at 2.9 mg/kg with resolution of peritoneal disease. PD, progressive disease; SD, stable disease.

- Disease control rate (CR+PR+SD) was 61% at ≥ 16 weeks and 55% at ≥ 24 weeks, with 3 patients on treatment at ≥ 74 weeks (**Figure 3**)

Figure 3. Treatment duration[a] and response in RECIST-evaluable patients treated with STRO-002 ≥ 2.9 mg/kg Q3W (N = 31)



[a]Duration calculated as date of PD or time from first dose to last dose given (including 4 patients deriving clinical benefit post progression per investigator assessment).

- Based on Kaplan-Meier estimates, median PFS and median DOR were 31.1 and 25 weeks, respectively (**Table 3**)

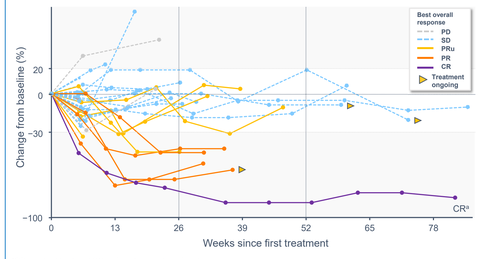
Table 3. Kaplan-Meier estimates of PFS and DOR[a]

Endpoint		Median (95% CI)
PFS, weeks	(N = 39)	31.1 (19.6, 47.0)
DOR,[a] weeks	(N = 5)	25 (8.8, NE)

[a]DOR for confirmed responses. NE, not estimable.

- Deepening responses in patients with tumor regression or a trend toward disease control over time were observed in most patients (**Figure 4**)

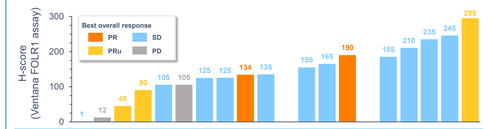
Figure 4. Change in sum of diameters for target lesions over time (N = 31)



[a]CR in patient treated at 2.9 mg/kg with resolution of peritoneal disease.

- Responses and antitumor activity were observed across various FRα expression levels assessed by immunohistochemistry (**Figure 5**)

Figure 5. FRα expression by immunohistochemistry[a] in individual patients treated with STRO-002 ≥ 2.9 mg/kg Q3W (N = 18)



FOLR1 PS2+ category	Weak/absent expression	Moderate expression	High expression
PR	1	1	0
PRu	2	0	1
SD	5	2	4
PD	2	0	0

[a]Assessed by Ventana FOLR1 expression assay based on available archival tissue from dose-escalation patients and scored using H-score and PS2 methods. FOLR1, folate receptor alpha.

- Pharmacokinetics: maximum plasma concentrations of STRO-002 were achieved by the end of the 1-hour infusion; exposure increased in a dose-proportionate manner

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