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Luveltamab tazevibulin, an anti-folate receptor alpha antibody-drug conjugate, in combination with bevacizumab in patients with recurrent high-grade epithelial ovarian cancer: STRO-002-GM2 phase 1 study

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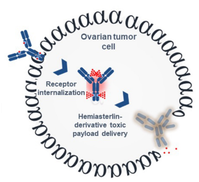
INTRODUCTION

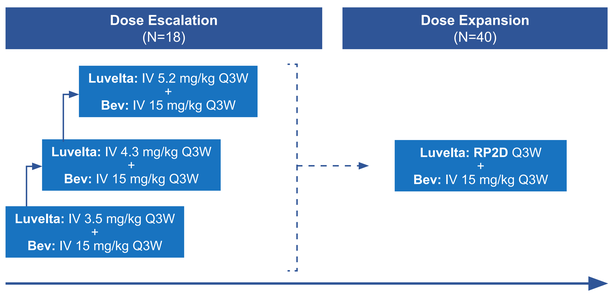
- Folate receptor alpha (FRα) is overexpressed in epithelial ovarian cancer (EOC), making it a favorable therapeutic target for recurrent EOC, an area of high unmet need, with limited disease control and survival in the platinum-resistant setting[1,2]
- **Luveltamab tazevibulin (luvelta; STRO-002)** is a FRα antibody-drug conjugate with a stable cleavable linker and a 3-aminophenyl hemiasterlin warhead that induces cytotoxic and immunogenic cell death[3]
- Luvelta monotherapy demonstrated encouraging antitumor activity and a manageable safety profile in the phase 1, open-label STRO-002-GM1 (NCT03748186) study in patients with recurrent EOC[4]
- Luvelta combined with bevacizumab (bev) has shown increased antitumor effects (vs luvelta alone) in ovarian cancer xenograft models, and preliminary clinical data suggest increased activity of the combination[5]
- Herein, we report the outcomes from the escalation portion of the ongoing phase 1/1b trial (NCT05200364) evaluating the recommended phase 2 dose (RP2D), safety, and antitumor activity of luvelta in combination with bev in patients with recurrent EOC
- Expansion at RP2D is ongoing; an additional 23 patients have been enrolled to date



METHODS

- STRO-002-GM2 is a global phase 1/2a, open-label, multicenter, dose-escalation and dose-expansion study including sites in US, Spain, Italy, and France (planned)
- Dose escalation employed a standard 3+3 design, with a 21-day dose-limiting toxicity (DLT) assessment period to determine the RP2D (**Figure 1**) for evaluation in dose expansion
- FRα expression data were not required for study entry; expression was determined retrospectively by immunohistochemistry, using VENTANA FOLR1 [FOLR1-2.1] RxDx Assay (Ventana Medical Systems, Roche Labs)
- Primary endpoints are incidence and severity of treatment-emergent adverse events (TEAEs), DLTs, RP2D, and overall response rate (ORR)

Figure 1. Study Schema



Bev, bevacizumab; IV, intravenous; Luvelta, luveltamab tazevibulin; Q3W, every 3 weeks; RP2D, recommended phase 2 dose.

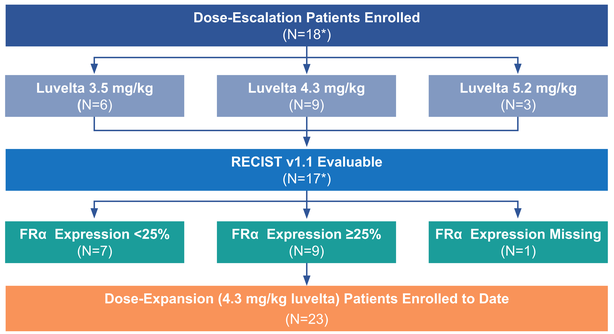
Key Inclusion Criteria

- Adults (≥18 years) with ECOG PS 0-1, high-grade serous EOC, fallopian tube, or primary peritoneal cancer, and RECIST v1.1 evaluable disease
- Relapse/progression on the last treatment and 1 of the following:
  - a) primary platinum refractory and received ≤2 prior regimens;
  - b) platinum resistant and received 1-4 prior regimens; or
  - c) platinum sensitive and received 2-4 prior regimens

ECOG, Eastern Cooperative Oncology Group; EOC, epithelial ovarian cancer; PS, performance status; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

PATIENTS

Figure 2. Patient Distribution



Data cut off date: August 2nd, 2024.
*One patient from the dose-escalation phase remains on treatment.
FRα, folate receptor alpha; luvelta, luveltamab tazevibulin; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Patient Demographics and Disease Characteristics (N=18)	
Median age, years (range)	63 (47–74)
ECOG PS, n (%)	
0	10 (56)
1	8 (44)
Median number of prior therapies (range)	2 (1–4)
Prior bev, n (%)	10 (56)
Prior PARPi, n (%)	13 (72)
Prior platinum, n (%)	18 (100)
BRCA positive, n (%)	2 (11)
Ascites, n (%)	5 (28)
PSOC	3 (17)

Data cut off date: August 2nd, 2024.
Bev, bevacizumab; *BRCA*, BReast CAncer gene; ECOG, Eastern Cooperative Oncology Group; PARPi, poly (ADP-ribose) polymerase inhibitor; PS, performance status; PSOC, platinum-sensitive ovarian cancer.

SAFETY

- The 4.3 mg/kg dose was selected for evaluation in the expansion phase
- At the 5.2 mg/kg dose, 1 out of 3 patients enrolled experienced a DLT of grade 3 nausea and a DLT of grade 4 decreased appetite on C1D11
- 9 (50%) patients experienced a TEAE leading to luvelta dose reduction; the most frequent TEAE leading to dose reduction was neutropenia
- 8 (44%) patients experienced treatment-related AEs leading to luvelta discontinuation
- Two deaths occurred in the dose-escalation phase:
  - Grade 5 non-neutropenic sepsis (C2): assessed as doubtfully related to luvelta and possibly related to bev; the probable cause of sepsis was malignant bowel perforation caused by progressive disease
  - Grade 5 sepsis (C12): occurred after the patient underwent a diabetic foot ulcer drainage procedure; considered not drug-related by the investigator (related to skin infection), but the sponsor upgraded attribution to possibly related
    - Safety guidelines were updated to advise that patients be evaluated by their oncologist prior to undergoing any surgical procedure

SAFETY

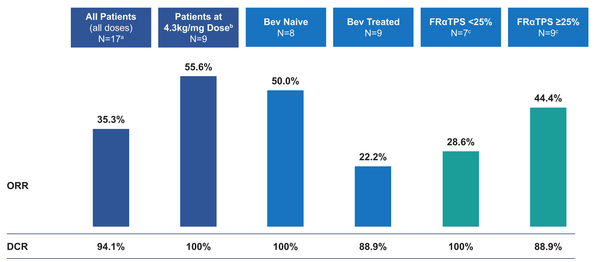
TEAEs >25% Incidence (Any Grade and Grade ≥3) (N=18)		
n, (%)	Any Grade	Grade ≥3
Patients with ≥1 TEAE	18 (100)	13 (72)
Neutropenia[a]	13 (72)	8[b] (44)
Constipation	11 (61)	1 (6)
Nausea	11 (61)	1 (6)
Arthralgia	11 (61)	0
Asthenia	8 (44)	2 (11)
Abdominal pain	7 (39)	1 (6)
Diarrhea	7 (39)	0
Fatigue	7 (39)	0
Aspartate aminotransferase increased	6 (33)	0
Headache	6 (33)	0
Thrombocytopenia	5 (28)	1 (6)
Vomiting	5 (28)	1 (6)
Platelet count decreased	5 (28)	1 (6)
Myalgia	5 (28)	0

Data cut off date: August 2nd, 2024.
[a]Neutropenia included the following preferred terms: neutropenia, febrile neutropenia, and neutrophil count decrease. [b]Of the 8 grade ≥3 neutropenia events, 1 event was febrile neutropenia.
TEAE, treatment-emergent adverse event.

EFFICACY

- **Figure 3** summarizes the response outcomes in the dose escalation, showing antitumor activity in all groups of patients
- An ORR of 35.3% (95% CI: 14.2, 61.7) was observed in the overall population with a median duration of response of 9.3 months (95%CI: 5.1, not reached)
- At the RP2D (4.3 mg/kg), 5 of 9 patients had a response; no patients had a response at 3.5 mg/kg and 1 (50%) patient had a response at 5.2 mg/kg

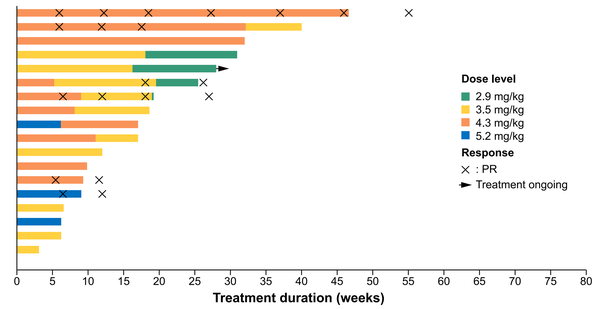
Figure 3. Response Outcomes in Dose Escalation



Data cut off date: August 2nd, 2024.
[a]One patient was not evaluable for response; [b]Selected RP2D; [c]FRα expression missing for 1 patient.
Responses were assessed in patients with baseline and post-treatment assessments (N=17).
Bev, bevacizumab; CI, confidence interval; DCR, disease control rate; FRα, folate receptor alpha; ORR, overall response rate; RP2D, recommended phase 2 dose; TPS, tumor proportion score.

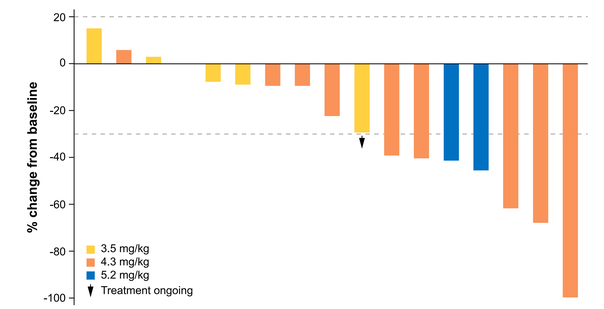
EFFICACY

Figure 4. Duration of Treatment and Responses (N=18)



Data cut off date: August 2nd, 2024.
PR, partial response.

Figure 5. Maximum Reduction in Target Tumor Lesions (N=17)



Data cut off date: August 2nd, 2024.

CONCLUSIONS

- Luvelta plus bevacizumab demonstrated encouraging antitumor activity irrespective of FRα expression and prior bev treatment
- Luvelta + bev had no new safety signals vs either agent alone
- These early data in combination may offer a non-biomarker driven approach to treat patients with relapsed/recurrent EOC
- The expansion phase of the study is accruing at the selected luvelta dose of 4.3 mg/kg in combination with bev; 23 patients have been enrolled to date

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Disclosures

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