Luveltamab Tazevibulin (STRO-002), an Anti-Folate Receptor Alpha Antibody Drug Conjugate, Demonstrates Clinical Activity in Recurrent Epithelial Endometrial Cancer: STRO-002-GM1 Phase 1 Dose Expansion

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Declaration of Interests

Bhavana Pothuri, MD

- Research support: AstraZeneca, Clovis Oncology, Tesaro/GSK, ImmunoGen, Onconova, Roche/Genentech, SeaGen, Merck, Mersana, Celsion/Imunon, Karyopharm, Sutro, Imab, Toray
- Advisory board: Clovis Oncology, Tesaro/GSK Inc, Lilly/AstraZeneca, Merck, Eisai, Mersana, Sutro, SeaGen, Imvax, GOG Foundation

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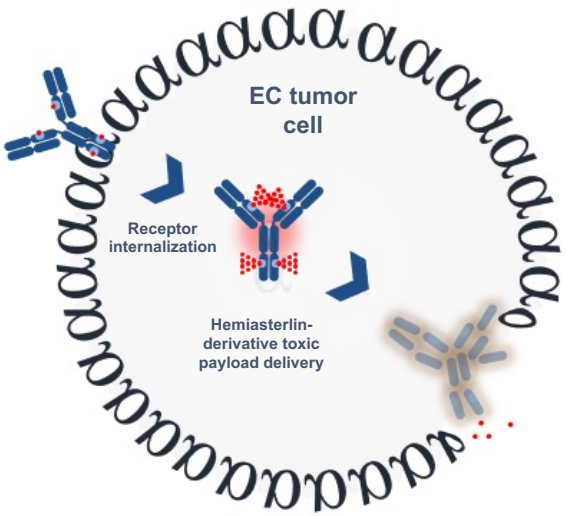
Luveltamab Tazevibulin (Luvelta), an ADC Directed Against Folate Receptor Alpha (FolRα), Has Potential as Targeted Therapy for Recurrent FolRα-Expressing EC

- **Endometrial cancer (EC) is the only gynecologic malignancy with increasing incidence and mortality[1]**
  - Estimated incidence in the EU: 92,746 pts with 23,047 deaths (2022)[2] and in the US: 66,000 pts with 13,030 deaths (2023)[3]
- Disease control and survival with chemotherapy for recurrent EC are limited (ORR ≈15%, mPFS ≈3.8 months, mOS <12 months)[4]
- Folate receptor alpha (FolRα) is a validated anti-tumor target in ovarian cancer that is overexpressed in EC compared with normal tissue[5]
- **Luvelta is a FolRα-targeting antibody drug conjugate (ADC) with a hemiasterlin cytotoxic warhead designed using site-specific conjugation and a cell-free synthesis platform to induce cytotoxic and immunogenic cell death[6]**
- **Luvelta has demonstrated anti-tumor activity in patients with > 25% FolRα-expressing recurrent epithelial ovarian cancer (EOC) in the STRO-002-GM1 phase 1 dose escalation/expansion study[7]**

Luveltamab Tazevibulin (Luvelta) or STRO-002



Designed to target a broad range of FolRα-expressing tumors

1.Siegel RL, et al. *CA Cancer J Clin.* 2023;73(1):17–48. 2. European Cancer Information System (ECIS). https://ecis.jrc.ec.europa.eu. Accessed 11 Oct 2023. 3. American Cancer Society Cancer Statistics 2023. https://www.cancer.org. Accessed 08 Sep 2023. 4. Makker V, et al. *N Engl J Med.* 2022;386(5):437–448. 5. Despierre E, et al. *Gynecol Oncol.* 2013;130:192–199. 6. Li X, et al. *Mol Cancer Ther.* 2023;22:155–167. 7. Oaknin A, at al. Presented at ASCO 2023 Annual Meeting; June 2–6, 2023; Chicago, IL. Abstract 5508.
ORR, overall response rate; mPFS; median progression free survival; mOS, median overall survival.

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STRO-002-GM1: Phase 1 Dose-Expansion Cohort of Luvelta in Recurrent EC

Key Inclusion and Exclusion Criteria

- Epithelial endometrial cancer
  - Excluded: leiomyosarcoma, stromal sarcomas and carcinosarcomas
- **≥1% FolRα expression by central IHC**
- Recurrent disease
  - **≥1 platinum-based chemotherapy or 1 immunotherapy-based regimen**
  - **≤3 prior regimens**
- At least 1 target lesion

17 Patients Enrolled

Luvelta Dosing Schedule

- Q3W cycles
- **5.2 mg/kg** unless prior pelvic XRT, then **4.3 mg/kg** X 2 cycles with option to dose escalate to 5.2 mg/kg

Endpoints

- Safety
- PK
- Anti-tumor activity assessed by ORR, DOR and PFS by RECIST v1.1
- CA-125

ClinicalTrials.gov NCT03748186

DOR, duration of response; IHC, immunohistochemistry; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetic; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; XRT, radiotherapy.

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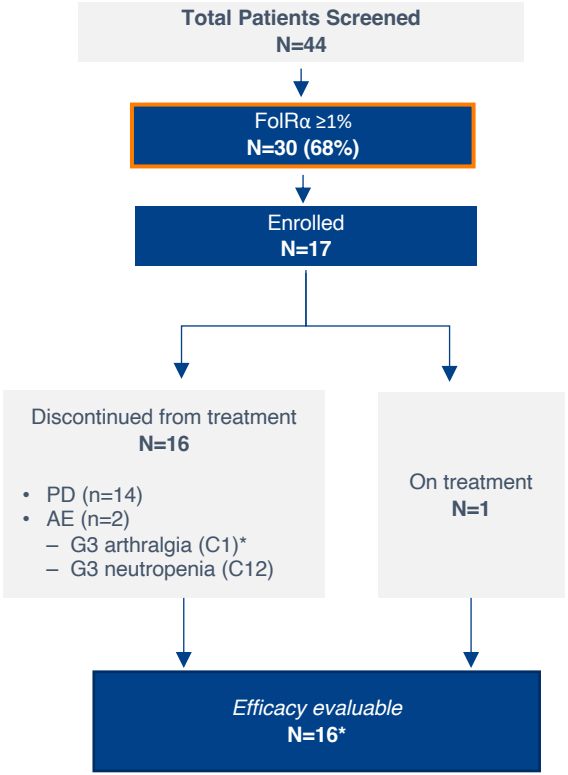
Patient Characteristics, Disposition, and Study Drug Exposure



Baseline Characteristics	Total N=17
Median age (range), years	68 (60–79)
Race, n (%)	
Asian	0
Black or African America	1 (6)
White	15 (88)
Unknown	1 (6)
Ethnicity, n (%)	
Hispanic or Latino	1 (6)
Not Hispanic or Latino	16 (94)
Median time since diagnosis (range), years	1.9 (0.6–14.5)
Median prior lines of therapy (range)	2 (1–3)
FolRα expression for enrolled pts, n (%)	
≥1%-25%	10 (59)
26-49%	4 (23)
50-74%	1 (6)
≥ 75%	2 (12)
ECOG PS, n (%)	
0	8 (47)
1	9 (53)
Tumor histology, n (%)	
Endometrioid	10 (59)
Serous	5 (29)
Mixed endometrioid/serous	1 (6)
Unknown	1 (6)
Prior platinum, n (%)	17 (100)
Prior PD-1/PD-L1 inhibitor, n (%)	4 (24)
Prior pelvic irradiation	9 (53)

*1 patient discontinued due to grade 3 arthralgia, prior to post-baseline scan. AE, adverse event; C, cycle; ECOG PS, Eastern Cooperative Oncology Group performance status; G, grade; PD, progressive disease; PD-L1, programmed death ligand 1.

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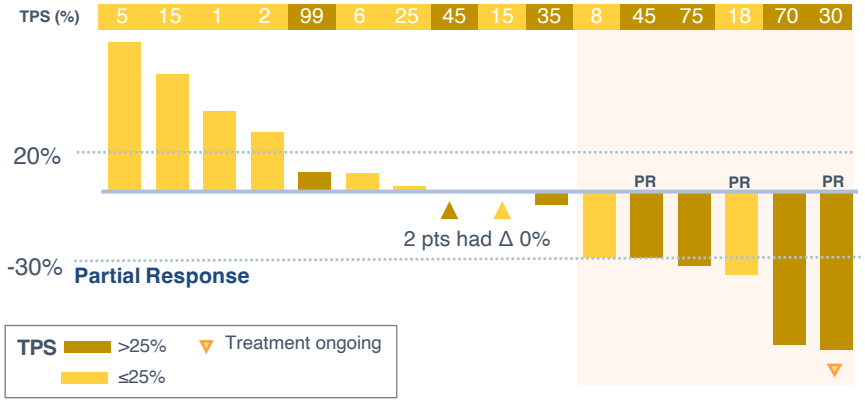
Luvelta Showed Early Evidence Of Anti-tumor Activity in FolRα Expressing EC

Maximum Reduction in Target Lesions*

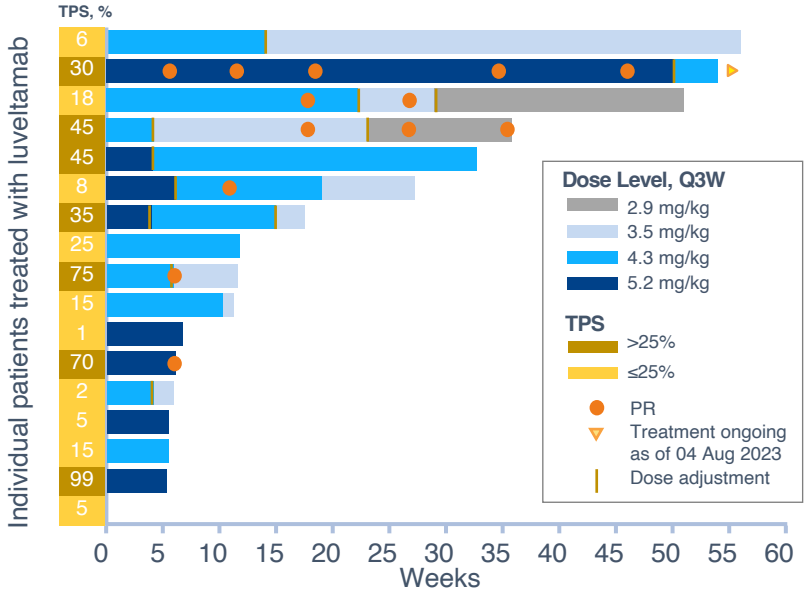


Anti-tumor Activity*

n (%)	Overall FolRα ≥1% (n=16)	FolRα ≤25% (n=9)	FolRα >25% (N=7)
PR	3 (19)	1 (11)	2 (29)
SD†	8 (50)	4 (44)	4 (57)
PD	5 (31)	4 (44)	1 (14)
DCR	11 (69)	5 (56)	6 (86)

†3 unconfirmed PRs

Treatment Duration and Dose Modifications



- Median exposure (range): 12 (3–53) weeks
- 5 of 17 (29%) patients received ≥5 cycles
- Median follow-up: 10.1 months

Data cutoff: 04 August 2023. *n=16 response evaluable patients. DCR, disease control rate; EC, endometrial cancer; PR, partial response; Q3W, every 3 weeks; TPS, tumor proportion score.

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TEAEs Consisted of Hematologic Events, Gastric Events and Arthralgia

No New Safety Signals Observed in EC Compared to Prior Data in EOC

TEAEs any grade (>25%)

TEAEs, n (%)	4.3 mg/kg (n=9)		5.2 mg/kg (n=8)		Total (n=17)	
	Any grade*	Grade ≥3	Any grade	Grade ≥3	Any grade*	Grade ≥3
Patients reporting at least 1 event	9 (100.0)	8 (88.9)	8 (100.0)	7 (87.5)	17 (100.0)	15 (82.2)
Anemia	6 (66.7)	2 (22.2)	7 (87.5)	2 (25.0)	13 (76.5)	4 (23.5)
Arthralgia	5 (55.6)	2 (22.2)	7 (87.5)	1 (12.5)	12 (70.6)	3 (17.6)
Neutropenia†	7 (77.8)	6 (66.7)	4 (50)	3 (37.5)	11 (64.7)	9 (52.9)
Nausea	4 (44.4)	0	6 (75)	1 (12.5)	10 (58.8)	1 (5.9)
Decreased appetite	4 (44.4)	0	6 (75)	0	10 (58.8)	0
Asthenia	5 (55.6)	1 (11.1)	4 (50)	0	9 (52.9)	1 (5.9)
Aspartate aminotransferase increased	4 (44.4)	0	5 (62.5)	0	9 (52.9)	0
Constipation	3 (33.3)	0	3 (37.5)	0	6 (35.3)	0
Alanine aminotransferase increased	3 (33.3)	0	3 (37.5)	0	6 (35.3)	0
Fatigue	2 (22.2)	1 (11.1)	3 (37.5)	0	5 (29.4)	1 (5.9)
Platelet count decreased	2 (22.2)	0	3 (37.5)	1 (12.5)	5 (29.4)	1 (5.9)
Myalgia	2 (22.2)	0	3 (37.5)	0	5 (29.4)	0
Neuropathy‡	3 (33.3)	0	2 (25)	0	5 (29.4)	0
Alopecia	3 (33.3)	0	2 (25)	0	5 (29.4)	0

*Any-grade AE >25%. †Neutropenia included the following preferred terms: neutropenia, febrile neutropenia, and neutrophil count decreased. ‡Neuropathy included the following terms: neuropathy peripheral and peripheral sensory neuropathy. TEAE, treatment-emergent adverse event.

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Conclusions

- Recurrent EC had a high incidence of FolRα expression ≥1%
  - 68% among 44 patients screened in this trial

- Luvelta (STRO-002) demonstrated encouraging preliminary anti-tumor activity in patients with FolRα-expressing EC with minimum and higher expression levels
  - **PR in 29% with DCR† of 86% (FolRα >25%)**
  - **PR in 19% with DCR† of 69% (FolRα ≥1%)**

- The safety profile of Luvelta was predictable, and AEs were manageable
  - The most common TEAEs were neutropenia, anemia, and arthralgia
  - No new safety signals (consistent in patients with EOC and EC)

- Luvelta may offer a targeted treatment option and warrants further development for recurrent EC

†3 SDs were unconfirmed PRs (2 in FolRα >25% and 1 in FolRα ≤ 25%). AE, adverse event; DCR, disease control rate; EC, endometrial cancer; EOC, epithelial ovarian cancer PR, partial response; TEAE, treatment emergent adverse event.

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