NEW DRUG APPROVAL

Brand Name	Elahere™
Generic Name	mirvetuximab soravtansine-gynx
Drug Manufacturer	ImmunoGen, Inc

New Drug Approval

FDA approval date: November 14, 2022

Review designation: N/A; Orphan

Type of review: Biologic License Application (BLA): 761310

Dispensing restriction: N/A

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Ovarian cancer is cancer that affects one or both ovaries. Ovarian cancer is not common. But because ovarian cancer often goes undetected until it is in an advanced stage, it is the number one cause of deaths from gynecologic cancer in the United States.

"Platinum resistant" ovarian cancer was historically defined as disease recurrence within 6months of completion of first-line platinum-based chemotherapy, although this is now more broadly applied to also include patients progressing within 6months after multiple lines of chemotherapy. However, this definition ignores the heterogeneity and complexity of the spectrum of diseases that comprise "platinum resistant ovarian cancer" (PROC) and is innately flawed as it was initially derived using methods of detection of recurrence that would now be regarded as outdated. The outcome of patients with PROC is generally poor, with low response rates to further chemotherapy and a median survival of less than 12months, but this is unpredictable and can be quite variable from study to study. This review outlines the complexity of PROC, examines how these impacts on the interpretation of the results of clinical trials, and explores how the definition may be improved. We also briefly describe the mechanisms of platinum resistance, the results of clinical trials to date as well as treatment options for patients with PROC and highlight the need for better methods of assessing clinical benefit in this poor prognostic subgroup of patients.

Ovarian cancer ranks fifth in cancer deaths among women, accounting for more deaths than any other cancer of the female reproductive system. A woman's risk of getting ovarian cancer during her lifetime is about 1 in 78. Her lifetime chance of dying from ovarian cancer is about 1 in 108. (These statistics don’t count low malignant potential ovarian tumors.)

This cancer mainly develops in older women. About half of the women who are diagnosed with ovarian cancer are 63 years or older. It is more common in white women than African American women.

The American Cancer Society estimates for ovarian cancer in the United States for 2022 are:

- About 19,880 women will receive a new diagnosis of ovarian cancer.
- About 12,810 women will die from ovarian cancer.

Efficacy

The efficacy of Elahere™ was evaluated in Study 0417 (NCT04296890), a single-arm trial of patients with FRα positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer (n=106). Patients were

permitted to receive up to three prior lines of systemic therapy. All patients were required to have received prior bevacizumab. The trial enrolled patients whose tumors were positive for FRα expression as determined by the VENTANA FOLR1 (FOLR1-2.1) RxDx Assay. Patients were excluded if they had corneal disorders, ocular conditions requiring ongoing treatment, Grade >1 peripheral neuropathy, or non-infectious interstitial lung disease.

Patients received Elahere™ 6 mg/kg (based on adjusted ideal body weight) as an intravenous infusion every 3 weeks until disease progression or unacceptable toxicity. Tumor response assessments occurred every 6 weeks for the first 36 weeks and every 12 weeks thereafter.

The major efficacy outcome measures were investigator-assessed overall response rate (ORR) and duration of response (DOR) evaluated according to Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1.

The efficacy evaluable population included 104 patients with platinum-resistant disease, who had measurable disease, and received at least one dose of Elahere™. In these 104 patients, the median age was 62 years (range: 35 to 85); 96% were White, 2% were Asian, and 2% did not have race reported. Two percent of patients were Hispanic or Latino. All patients had an ECOG PS of 0 (57%) or 1 (43%). Ten percent of patients had received 1 prior line of systemic therapy, 39% of patients had received 2 prior lines of systemic therapy, and 50% of patients had received 3 prior lines of systemic therapy. All patients had received prior bevacizumab and 47% had received a prior PARP inhibitor.

Table 1: Efficacy Results in Study 0417

	Elahere™ (N=104)
Confirmed Overall Response Rate[a] (95% CI)	31.7% (22.9, 41.6)
Complete response rate	4.8%
Partial response rate	26.9%
Duration of Response	N=33
Median duration of response, months (95% CI)	6.9 (5.6, 9.7)

[a] Investigator assessment.
Response assessment results using independent radiology review were consistent with investigator assessment.

Safety

ADVERSE EVENTS

The most common (≥20 %) adverse reactions, including laboratory abnormalities, were vision impairment, fatigue, increased aspartate aminotransferase, nausea, increased alanine aminotransferase, keratopathy, abdominal pain, decreased lymphocytes, peripheral neuropathy, diarrhea, decreased albumin, constipation, increased alkaline phosphatase, dry eye, decreased magnesium, decreased leukocytes, decreased neutrophils, and decreased hemoglobin.

WARNINGS & PRECAUTIONS

- Pneumonitis: Withhold Elahere™ for persistent or recurrent Grade 2 pneumonitis and consider dose reduction. Permanently discontinue Elahere™ for Grade 3 or 4 pneumonitis.
- Peripheral Neuropathy: Monitor patients for new or worsening peripheral neuropathy. Withhold dosage, dose reduce, or permanently discontinue Elahere™ based on the severity of peripheral neuropathy.

- Embryo-Fetal Toxicity: Elahere™ can cause fetal harm. Advise of the potential risk to a fetus and to use effective contraception.

CONTRAINDICATIONS

None reported.

Clinical Pharmacology

MECHANISMS OF ACTION

Mirvetuximab soravtansine-gynx is an antibody-drug conjugate (ADC). The antibody is a chimeric IgG1 directed against folate receptor alpha (FRα). The small molecule, DM4, is a microtubule inhibitor attached to the antibody via a cleavable linker. Upon binding to FRα, mirvetuximab soravtansine-gynx is internalized followed by intracellular release of DM4 via proteolytic cleavage. DM4 disrupts the microtubule network within the cell, resulting in cell cycle arrest and apoptotic cell death.

Dose & Administration

ADULTS

- Administer Elahere™ as an intravenous infusion only after dilution in 5% Dextrose Injection, USP. Elahere™ is incompatible with normal saline.
- The recommended dose of Elahere™ is 6 mg/kg adjusted ideal body weight (AIBW) administered once every 3 weeks (21-day cycle) as an intravenous infusion until disease progression or unacceptable toxicity.
- Premedicate with a corticosteroid, antihistamine, and antipyretic. Premedicate with an antiemetic, ophthalmic topical steroids, and lubricating eye drops.

PEDIATRICS

N/A

GERIATRICS

Refer to adult dosing.

RENAL IMPAIRMENT

N/A

HEPATIC IMPAIRMENT

N/A

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

Injection: 100 mg/20 mL (5 mg/mL) in a single-dose vial.