Mirvetuximab soravtansine-gynx (ELAHERE) for Epithelial Ovarian Cancer (EOC)
National Drug Mini-monograph
March 2025

VA Pharmacy Benefits Management Services and National Formulary Committee

The purpose of VA National Formulary Committee drug monographs is to provide a focused drug review for making formulary decisions. The Product Information or other resources should be consulted for detailed and most current drug information.

FDA APPROVAL INFORMATION

Description / MOA	Mirvetuximab soravtansine-gynx (MIR-GYNX) is a Folate receptor alpha (FRα)-directed antibody and microtubule inhibitor (DM4) and a linker, sulfo-SPDB. Upon binding to FRα, MIR-GYNX is internalized followed by intracellular release of DM4, which disrupts the microtubule network in the cell.
Indication Under Review[1]	FRα positive, platinum-resistant epithelial ovarian, fallopian tube or primary peritoneal cancer in adults who have received 1-3 prior systemic treatment regimens. Select patients based on an FDA-approved test. Approved under accelerated approval 2022, full approval March 2024
Dosage Regimen	Intravenous infusion of 6 mg/kg adjusted ideal body weight every 3 weeks until disease progression or unacceptable toxicity.
Dosage Forms Under Review	Single-dose vial (100mg/20 mL) for dilution and intravenous infusion

EFFICACY CONSIDERATIONS

Trial	**SORAYA (NCT04296890) Phase 2**	**FORWARD 1 (NCT02631876) Phase 3**
Design	Single-arm trial (n=104)	Randomized (2:1), open-label trial (n=366)
Population	High-grade serious platinum-resistant ovarian cancer with high FRα expression and 1-3 prior therapies (prior bevacizumab required).	High-grade FRα+, platinum-resistant ovarian, fallopian tube or primary peritoneal cancer (EOC) and 1-3 prior therapies.
Intervention	6 mg/kg (aIBW) MIR-GYNX every 3 weeks until unacceptable toxicity, progressive disease, withdrawal or death	6 mg/kg (aIBW) MIR-GYNX every 3 weeks until disease progression or unacceptable toxicity
Comparator	None	Chemotherapy: investigator's choice of paclitaxel, pegylated liposomal doxorubicin or topotecan
Demographics	mAge 62 yrs (range 35-85); 96% white, 2% Asian, 2% AA. Primary dx: 80% epithelial ovarian, 8% fallopian tube, 11% primary peritoneal. ECOG PS 0 (57%) or 1 (43%). Lines of prior systemic therapy: One: 9%,2: 39%, 3: 51%. All had received prior bevacizumab and 47% a prior PARP inhibitor. 20% had BRCA mutations	mAge 64 (range 34-89) vs. 64 (range 31-86). Primary diagnosis high-grade serous EOC 84% and 89%, fallopian tube Ca 6% vs. 4%, primary peritoneal 11% vs. 7%. ECOG PS 0 57% vs. 60% and PS 1 43% vs. 48%. 1 or 2 previous lines of therapy 64% vs. 63%. Prior exposure to therapy: Paclitaxel 96% each, bevacizumab 49% vs. 47%, PARP inhibitor 18% vs. 16%. **High FRα expression subgroup 60% (147 MIR-GYNX, 71 Chemo).**
Results	Primary Outcome: Objective response rate (ORR) and duration of response (DOR)	Progression free survival ITT (all randomized) and high FRα subgroup (≥75% tumor cells staining visible). Secondary = ORR, OS. Median duration follow up 12.5 months for both groups

Outcome	**MIR-GYNX (n=104)**
ORR (95% CI) CR PR	32%, (23, 42) 5% 27%
mDOR, months (n=33)	6.9 (5.6, 9.7)

Outcome	**MIR-GYNX (n=248)**	**Chemo (n=118)**	**HR (95% CI) p value**
mPFS, mos.	4.1	4.4	0.98 (0.73, 1.31) P=0.897
mPFS, FRα subgroup, mos.	4.8	3.3	0.69 (0.48, 1.00) P=0.049 (NS)
ORR, ITT	22%	12%	P=0.015
CA-125 responses	51%	27%	P<0.001
OS, ITT, mos.	16.4	14	0.8 (0.58, 1.15)
OS, FRα subgroup	17.3	12	0.7 (0.5, 1.0)

Trial	**MIRASOL (NCT04209855) Phase 3**
Design	Randomized (2:1), open-label trial (n=453)
Population	FRα+, Platinum-resistant FRα+ EOC, primary peritoneal or fallopian tube cancer and 1-3 prior therapies.
Intervention	2:1 randomization MIR-GYNX 6 mg/kg (aIBW) every 3 weeks
Comparator	Investigators's choice of paclitaxel, pegylated liposomal doxorubicin or topotecan
Demographics	mAge 64 (range 32-88) vs. 62 (range 29-87), 69% and 64% white, 4% and 2% black, 12% and 11% Asian. Primary diagnosis: high-grade serous EOC 80% vs. 81%, fallopian tube Ca 12% vs. 10%, primary peritoneal 7% vs. 9%. ECOG PS 0 (57% vs. 53%), 1 (43% vs. 45%) or 2 (0% vs. 1%). BRCA mutation 15% vs. 16%. Prior lines of therapy: 1 (13% vs. 15%), 2 (40% vs. 39%) or 3 (48% vs. 46%). All prior taxane therapy. Others: bevacizumab (61% vs. 63%), PARP inhibitor (55% vs. 56%), doxorubicin (or liposomal) (57% vs. 59%)
Results	Primary outcome: investigator assessed progression-free survival (PFS), ORR and overall survival (OS). Median duration of treatment (safety population) 5 vs.3 months for a median of 7 vs. 3 cycles (range 1-39 and 1-19, respectively)

Outcome	**MIR-GYNX (n=227)**	**Chemo (n=226)**	**HR (95% CI) / P value**
mPFS, mos. (95% CI)	5.6 (4.3, 5.9)	4.0 (2.9, 4.5)	0.65 (0.52, 0.81) P<0.001
mOS, mos. (95% CI)	16.5 (14.5, 24.6)	12.8 (10.9, 14.4)	0.67 (0.5, 0.89) P= 0.005
ORR (95% CI) CR PR	42% (36, 49) 5% 37%	16% (12, 22) 0% 16%	P<0.0001
mDOR, mos.	6.8 (5.6, 8.3)	4.5 (4.2, 5.8)	0.62 (0.4, 0.97)

SAFETY CONSIDERATIONS

Boxed Warnings	Ocular toxicity – Ocular AEs 59% of patients (11% Grade 3 and 0.3% Grade 4). Included blurred vision 48%, keratopathy 36%, cataract (16%), photophobia (14%) and eye pain (10%). Median time to first onset 5.1 wks. Complete resolution in 53%, partial 38%. Patients should be premedicated with lubricating eye drops and topical steroid eye drops
Contraindications	None
Other Warnings	Pneumonitis: 10% (1% Grade 3 and 0.1% Grade 4). MIR-GYNX should be held for Grade 2 pneumonitis until Grade 1 or lower and discontinued permanently in those with Grade 3 or 4. Peripheral neuropathy: 36% (3% Grade 3). Median time to onset 5.9 weeks. Complete resolution 23%, partial 12%. Depending on severity, consider withholding or reducing doses or discontinuation. Embryo-fetal toxicity: ermbryo-fetal harm possible when administered to pregnant woman. Patients should be advised of risks to a fetus and persons of reproductive potential advised to use effective contraception during treatment and for 7 months after the last dose
Top 5 AEs	(≥ 20% of patients in pooled safety data) increased AST / ALT, increased alkaline phosphatase, fatigue, blurred vision / keratopathy / dry eye, nausea, diarrhea, abdominal pain, vomiting, decreased appetite, constipation, peripheral neuropathy, musculoskeletal pain, decreased leukocytes/ lymphocytes/platelets/hemoglobin, decreased magnesium, decreased albumin. **In FORWARD 1:** AEs (≥ Grade 3) MIR-GYNX vs. chemo: 25% vs. 44%, dose reductions (20% vs. 30%) and discontinuation (5% vs. 8%) lower with MIR-GYNX and Chemo, respectively **In MIRASOL:** AEs (≥ Grade 3) MIR-GYNX vs. chemo: 42% vs. 54%, dose reductions (34% vs. 24%), dose delays / holds (54% vs. 54%) and discontinuation (9% vs. 16%)
Drug Interactions	Monitor closely for MIR-GYNX ADE with strong CYP3A4 inhibitors.

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VHA PLACE IN THERAPY

- High-grade, serous epithelial ovarian, fallopian tube and peritoneal carcinomas (HGSC) treated as a similar clinical entity and are most common histology accounting for the vast majority of HGSC and are typically diagnosed at an advanced stage with poor overall prognosis. Many patients respond to platinum-based chemotherapy but most will become refractory and single-agent chemotherapy (paclitaxel, liposomal doxorubicin or topotecan) is the standard treatment.
- MIR-GYNX targets a specific subset of patients with platinum-resistant ovarian, fallopian tube or primary peritoneal cancer with high FRα expression defined as $\geq$ 75% viable tumor cells with moderate (2+) or strong (3+) staining intensity.
- For this subset of patients, MIR-GYNX is associated with higher OS and PFS with a generally lower rate of adverse events than single-agent chemotherapy, but does have specific toxicities (ocular, peripheral neuropathy and pneumonitis) that need to be considered.
- Within the VA Clinical Pathway, mirvetuximab is preferred in platinum-refractory or platinum-resistant disease, but only those with FRα expression. Mirvetuximab is a category 2B recommendation in the NCCN Ovarian Cancer Guidelines (useful in certain circumstances).

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References

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2. Coleman R, Lorusso D, Oaknin A, et al., Mirvetuximab soravtansine in folate receptor alpha (FRα)-high platinum-resistant ovarian cancer: final overall survival and post hoc sequence of therapy subgroup results from the SORAYA trial. *Int J Gynecol Cancer* 2024;Online first. Doi:10.1136/ijgc-2024-005401.
3. Moore K, Oza A, Colombo N, et. al., Phase III, randomized trial of mirvetuximab soravtansine versus chemotherapy in patients with platinum-resistant ovarian cancer: Primary analysis of FORWARD I. *Ann Onc* 2021;32(6):757-65.
4. Moore KN, Angelergues A, Konecny G, et al. Mirvetuximab soravtansine in FRα-positive, platinum-resistant ovarian cancer. *N Engl J Med* 2023;389:2162-74.
5. NCCN Clinical Practice Guidelines in Oncology: Ovarian Cancer including fallopian tube cancer and primary peritoneal cancer. Version 3.2024 – July 15, 2024.
6. NCCN Clinical Practice Guidelines in Oncology: Ovarian Cancer including fallopian tube cancer and primary peritoneal cancer. NCCN Evidence Blocks. Version 3.2024 – July 15, 2024.

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