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Positive Quality Intervention: Mirvetuximab soravtansine-gynx (Elahere®) for Patients with Platinum-Resistant Ovarian, Fallopian tube, or Primary Peritoneal Cancer

Description: The purpose of this PQI is to discuss clinical considerations surrounding the use of mirvetuximab soravtansine-gynx for patients with platinum-resistant ovarian, fallopian tube, or primary peritoneal cancer.

Background: Epithelial ovarian cancer, including fallopian tube and primary peritoneal cancers, share similar histology and management.[1] Mirvetuximab soravtansine-gynx (MIRV) is an antibody-drug conjugate targeting folate receptor alpha (FRα), which is commonly overexpressed in ovarian cancer.[2,3,4] MIRV is indicated for the treatment of FRα-positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer in adults who have had 1-3 prior treatments.[2]

The phase 3 MIRASOL trial[5] (n=453) evaluated MIRV's efficacy and safety versus chemotherapy in patients with epithelial high-grade serous ovarian cancer with high FRα expression. The median progression-free survival (mPFS) was 5.62 months with MIRV compared to 3.98 months with chemotherapy. MIRV also improved objective response rate (ORR) and median overall survival, with rates of 42.3% versus 15.9% and 16.46 months versus 12.75 months, respectively. Common adverse events included blurred vision (41%), keratopathy (32%), abdominal pain (30%), and fatigue (30%).[5]

In the phase 1b/2 FORWARD II trial[6], MIRV plus bevacizumab (n=94) was evaluated as one of multiple combination cohorts in patients with platinum-resistant ovarian cancer with varying levels of FRα expression (≥ 25% tumor staining at ≥ 2+ intensity). The ORR was 44%, median response duration 9.7 months, and mPFS 8.2 months. While activity was observed across all levels of FRα expression, including patients with tumors expressing 25-49%, those with FRα expression ≥75% exhibited a higher ORR and longer mPFS vs. those with 50-74% expression.[6]

PQI Process:

1. **Verify FRα status ≥75% positive tumor cells**
    a. Mirvetuximab soravtansine-gynx is indicated for adult patients with platinum-resistant ovarian cancer whose tumors overexpress folate receptor alpha (FRα). FRα is a folate transport protein that is expressed in 80-90% patients with ovarian cancer and has limited expression in normal tissue. [3,7,8]

    FRα status is identified via the FDA-approved diagnostic VENTANA FOLR1 RxDx assay, which is a qualitative immunohistochemistry assay. Patients are deemed to be folate receptor positive if they have at least 75% of viable tumor cells with membrane staining at moderate and/or strong intensity levels as shown in the table below.[9] As FRα expression remains relatively unchanged[10-11], it may be tested at diagnosis or upon progression.

FOLR1 Status	Staining Description[9]
Positive	≥ 75% of viable tumor cells with moderate (2+) and/or strong (3+) membrane staining
Negative	< 75% of viable tumor cells with moderate (2+) and/or strong (3+) membrane staining

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2. **Calculate dosing using adjusted ideal body weight (AIBW)[12]**
    a. The recommended dose of mirvetuximab soravtansine-gynx is 6 mg/kg based on AIBW administered intravenously every 3 weeks. AIBW is calculated using the following formula:

    AIBW (kg) = IBW (kg) + 0.4 [Actual weight (kg) – IBW (kg)]

    Formula for ideal body weight used in clinical trials is as follows:

    [Female Ideal Body Weight (kg)] = 0.9 x height (cm) -92

    *Note this equation differs from the commonly utilized Devine formula of ideal body weight:
    [Female Ideal Body Weight (kg)] = 45.5kg + 2.3 kg (for each inch over 5 feet)

    NOTE: dose calculations may be variable depending on the ideal body weight equation the electronic medical record (EMR) uses. Doses calculated using the manufacturer recommended ideal body weight equation should be compared to the EMR dose calculation to identify discrepancies.

    b. Patients whose actual body weight is less than their ideal body weight received MIRV at the adjusted ideal body weight dose in the SORAYA trial. In clinical practice, it is up to provider discretion which dosing weight, actual body weight versus adjusted ideal body weight, to use to balance therapeutic efficacy and minimization of the risk of adverse effects.
3. **Preparation[2]**
    a. Mirvetuximab soravtansine-gynx is **only compatible with 5% dextrose** Injection, USP diluted to a final concentration of 1 mg/mL to 2 mg/mL.
    b. Available as preservative-free single-dose vials of 100mg/20mL stored refrigerated
    c. Allow vials to come to room temperature prior to dilution. Gently swirl vial. **DO NOT SHAKE**
    d. Follow hazardous handling and disposal procedures
4. **Administration[2]**
    a. Administer the following pre-medications at least 30 minutes prior to each Elahere® infusion
        i. Dexamethasone 10 mg IV
        ii. Diphenhydramine 25-50 mg PO/IV
        iii. Acetaminophen 325-650 mg PO/IV
        iv. 5-HT_3 serotonin receptor antagonist (i.e. ondansetron) 8 mg PO/IV (prior to each dose or as needed)
    b. Elahere® is administered IV via a 0.2 micron in-line filter
        i. **First dose:**
            1. Start at a rate of 1 mg/min for 30 minutes
            2. If well tolerated, may increase to 3 mg/min for 30 minutes
            3. If well tolerated, may increase to maximum rate of 5 mg/min for the remainder of the infusion.
        ii. **Subsequent infusions:** If no infusion-related reactions with the previous dose, subsequent infusions may be given at the maximum tolerated rate up to a maximum of 5 mg/min.
    c. **Only use 5% dextrose for flushing upon completion of infusion**

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5. **Monitoring**[2]
    a. Verify pregnancy status in females of childbearing potential
    b. CBC with differential to monitor for hematologic toxicity, including decreased neutrophils, platelets, and lymphocytes. Hold dose for Grade 3-4 hematologic toxicity
    c. CMP to monitor liver enzymes for hepatotoxicity. Avoid use in moderate to severe hepatic impairment (T-bili > 1.5x ULN)
    d. Electrolytes and replace as needed
    e. Review patient's medication list for drug-drug interactions. Strong CYP3A4 inhibitors may cause increased MIRV-associated adverse reactions.
    a. Monitor for new or worsening pulmonary symptoms or infiltrates on radiographic exam. Withhold therapy for grade 2 pneumonitis until resolution of ≤grade 1 then consider dose reduction
    b. Monitor for peripheral neuropathy and withhold, dose reduce, or permanently discontinue therapy based on severity.

Patient-Centered Activities[2]**:**

2. Provide Intravenous Chemotherapy Education (IVE) sheets and review with the patient.
3. Educate patient on required eye care during treatment:
    a. WARNING : Elahere can cause severe ocular toxicities, including visual impairment, keratopathy, dry eye, photophobia, eye pain, and uveitis.
    b. Eye examination by ophthalmologist or optometrist (including visual acuity and slit lamp exam) before cycle 1 then at cycles 3, 5 and 7 is required, then as clinically indicated
    c. Avoid use of contact lenses. Administer prophylactic eye drops
        i. Instill steroid drops (prednisolone 1% or equivalent) into EACH eye
            1. Days 0 – 4: Instill 1 drop in each eye 6 times daily starting the day before infusion , Days 5 -8: Instill 1 drop in each eye 4 times daily
        ii. Instill preservative-free lubricating eye drops in each eye at least 4 times daily and as needed, waiting at least 10 minutes after steroid eye drop
4. Review Chemotherapy-Induced Nausea and Vomiting protocols.
5. Educate patients to report any new or worsening pulmonary symptoms such as cough or shortness of breath. Pneumonitis occurred in 10% of patients treated with mirvetuximab soravtansine-gynx.
6. Discuss Peripheral Neuropathy (PN) with patient. PN occurred in 36% of patients with a median time to onset of 5.9 weeks (0.1-126.7).
7. Infusion-Related Reactions: (8%) Educate patients to report symptoms during infusion if they occur.
8. Embryo-Fetal Toxicity: Use effective contraception during treatment and for 7 months after last dose
9. Patient Assistance: NCODA Financial Assistance Tool

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