CLINICAL VIGNETTE

Mirvetuximab Soravtansine in Platinum Resistant Ovarian Cancer

Kari Kubalanza, MD

Introduction

Ovarian cancer is the second most common gynecologic malignancy and the most common cause of gynecologic cancer death in the United States with 19,680 estimated new cases and 12,740 deaths estimated for the United States in 2024.[1] Presenting symptoms are nonspecific and include pelvic pain, bloating, urinary urgency or frequency, and gastrointestinal symptoms. And most women are diagnosed with advanced stage disease. Frontline treatment includes platinum-based chemotherapy. Unfortunately, the majority of women with advanced disease will relapse after platinum-based chemotherapy and require further treatment. Women with a platinum-free interval of less than six months are considered to have platinum-resistant disease with poor prognosis. The 5-year survival for platinum-resistant disease is approximately 50%,[1] and, improved treatment options are needed.

Case

A 55-year-old female with no significant past medical history presented to oncology with platinum resistant ovarian cancer. She initially presented to the emergency room in 2020 with several months of progressive abdominal pain. CT abdomen/pelvis demonstrated a 5cm left adnexal mass, diffuse peritoneal nodularity, and moderate ascites. CA-125 was elevated at 600. She underwent optimal cytoreduction with total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and tumor debulking of implants. Pathology revealed high grade serous ovarian carcinoma. Next generation sequencing was unremarkable with no targetable mutations, including BRCA and HRD negativity.

She was treated with 6 cycles of adjuvant carboplatin plus paclitaxel with normalization of CA-125. She was monitored closely, and CA-125 began to increase 9 months later. Imaging confirmed progression with new peritoneal nodularity and increased lymphadenopathy. She underwent treatment with carboplatin plus pegylated liposomal doxorubicin combined with bevacizumab for platinum-sensitive disease with good response. Unfortunately, she progressed 4 months later. Folate receptor alpha (FRα) testing was sent and confirmed positive, and she underwent treatment with Mirvetuximab soravtansine for platinum-resistant ovarian cancer.

Discussion

The Food and Drug Administration granted accelerated approval in November 2022 and full approval in March 2024 for Mirvetuximab soravtansine for adult patients with FRα positive (≥75% of cells with ≥2+ staining intensity), platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have received one to three prior systemic treatment regimens.[2-4] Mirvetuximab soravtansine is an antibody-drug conjugate with a folate receptor alpha directed antibody and microtubule inhibitor payload. FRα is commonly overexpressed on ovarian carcinomas and minimally expressed on normal tissues.[5] The recommended Mirvetuximab soravtansine dose is 6 mg/kg adjusted ideal body weight administered once every three weeks.

FDA approval was based on the MIRASOL trial, which showed improvement in overall survival (OS), progression free survival (PFS), and overall response rate (ORR). MIRASOL is a phase 3 randomized trial in FRα positive patients with platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer.[4] Four hundred fifty-three patients were randomized to receive Mirvetuximab soravtansine versus investigator's choice of chemotherapy (paclitaxel, pegylated liposomal doxorubicin, or topotecan) until disease progression or unacceptable toxicity. Median OS was 16.5 months in the Mirvetuximab soravtansine arm and 12.8 months in the chemotherapy arm (HR 0.67). Median PFS was 5.6 months in the Mirvetuximab soravtansine arm and 4.0 months (HR 0.65) in the chemotherapy arm and ORR was 42% and 16% (95% CI: 12, 22), respectively.

Mirvetuximab soravtansine is generally well tolerated. However, there is a boxed warning for ocular toxicity, including visual impairment, keratopathy, dry eye, photophobia, eye pain, and uveitis. It is recommended that patients undergo ophthalmic exam prior to initiation of Mirvetuximab soravtansine and every other cycle for the first 8 cycles, and as clinically indicated. Patient should also administer prophylactic artificial tears and ophthalmic topical steroids for the duration of treatment. The most common adverse reactions included fatigue, nausea/vomiting, diarrhea, ocular toxicity, electrolyte abnormalities, increased transaminases, peripheral neuropathy, musculoskeletal pain, myelosuppression (grade 3-4 rare), and decreased appetite. Pneumonitis is also a rare, life-threatening complication.

Conclusion

Platinum-resistant ovarian cancer has poor prognosis and needs better treatment options. Mirvetuximab soravtansine is a first-in-class antibody–drug conjugate targeting folate receptor α, a biomarker that is commonly overexpressed in ovarian cancer and minimally expressed on normal tissue. It was approved in 2022 for treatment of FRα positive platinum-resistant ovarian cancer. Mirvetuximab soravtansine showed a significant benefit over standard of care chemotherapy with respect to overall survival, progression free survival, and objective response. Overall, Mirvetuximab soravtansine is a well-tolerated treatment, but requires close ocular monitoring.

REFERENCES

1. NIH National Cancer Institute Surveillance, Epidemiology and End Results Program. Cancer Stat Facts: Ovarian Cancer. Available at: https://seer.cancer.gov/statfacts/html/ovary.html.
2. FDA U.S. Food & Drug Administration. Drugs. Available at: https://www.fda.gov/drugs.
3. **Moore KN, Oza AM, Colombo N, Oaknin A, Scambia G, Lorusso D, Konecny GE, Banerjee S, Murphy CG, Tanyi JL, Hirte H, Konner JA, Lim PC, Prasad-Hayes M, Monk BJ, Pautier P, Wang J, Berkenblit A, Vergote I, Birrer MJ**. Phase III, randomized trial of mirvetuximab soravtansine versus chemotherapy in patients with platinum-resistant ovarian cancer: primary analysis of FORWARD I. *Ann Oncol*. 2021 Jun;32(6):757-765. doi: 10.1016/j.annonc.2021.02.017. Epub 2021 Mar 2. PMID: 33667670.
4. **Moore KN, Angelergues A, Konecny GE, García Y, Banerjee S, Lorusso D, Lee JY, Moroney JW, Colombo N, Roszak A, Tromp J, Myers T, Lee JW, Beiner M, Cosgrove CM, Cibula D, Martin LP, Sabatier R, Buscema J, Estévez-García P, Coffman L, Nicum S, Duska LR, Pignata S, Gálvez F, Wang Y, Method M, Berkenblit A, Bello Roufai D, Van Gorp T; Gynecologic Oncology Group Partners and the European Network of Gynaecological Oncological Trial Groups**. Mirvetuximab Soravtansine in FRα-Positive, Platinum-Resistant Ovarian Cancer. *N Engl J Med*. 2023 Dec 7;389(23):2162-2174. doi: 10.1056/NEJMoa2309169. PMID: 38055253.
5. **Moore KN, Martin LP, O'Malley DM, Matulonis UA, Konner JA, Perez RP, Bauer TM, Ruiz-Soto R, Birrer MJ**. Safety and Activity of Mirvetuximab Soravtansine (IMGN853), a Folate Receptor Alpha-Targeting Antibody-Drug Conjugate, in Platinum-Resistant Ovarian, Fallopian Tube, or Primary Peritoneal Cancer: A Phase I Expansion Study. *J Clin Oncol*. 2017 Apr 1;35(10):1112-1118. doi: 10.1200/JCO.2016.69.9538. Epub 2016 Dec 28. PMID: 28029313; PMCID: PMC5559878.