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Navigating the Therapeutic Landscape of Platinum-Resistant Ovarian Cancer

Announcer:
Welcome to CE on ReachMD. This activity is provided by Prova Education. This episode is part of our MinuteCE curriculum.

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Dr. Liu:
This is a CE on ReachMD, and I'm Dr. Joyce Liu. In this brief lecture, I'll review the ongoing treatment challenges in platinum-resistant ovarian cancer and the need for novel biomarker-targeted therapies.

Effective treatments for platinum-resistant ovarian cancer remain an area of high unmet need in the ovarian cancer space. While newly diagnosed ovarian cancer has high response and remission rates to first-line therapy with surgery and combined platinum and taxane therapy, most of these cancers will unfortunately recur and will eventually develop resistance to platinum-based chemotherapies.

The NCCN Guidelines list a number of potential therapeutic regimens for platinum-resistant ovarian cancer. Among the preferred regimens are weekly paclitaxel, liposomal doxorubicin, and topotecan, each of which may be administered with or without bevacizumab based upon the findings from the AURELIA trial, which demonstrated that the addition of bevacizumab to these regimens improved response rates and progression-free survival in platinum-resistant ovarian cancer, although no improvement in overall survival was observed.

The addition of bevacizumab to chemotherapy in this setting does carry certain risks, including hypertension, proteinuria, and, most notably, GI perforation, which, in AURELIA, was observed in 2.2% of patients. Other preferred regimens in this setting include gemcitabine and mirvetuximab soravtansine for patients with folate receptor alpha high tumors, which I'll come back to shortly.

Unfortunately, although there are a number of options available as potential therapy for platinum-resistant ovarian cancer, historically we have seen that the activity of standard chemotherapy in this setting remains limited, with an observed response rate in phase 3 trials of only about 10% to 15% with a median progression-free survival of approximately 3 and a half months. Overall survival in these trials has also been limited, often just a little bit over a year.

The recently published results of the ROSELLA trial, which demonstrated improved progression-free survival with adding the anti-glucocorticoid agent, relacorilant, to nab-paclitaxel, compared to nab-paclitaxel alone, may further add to our available armamentarium.

Positive results have also been announced from the KEYNOTE-B96 trial of combined weekly paclitaxel and pembrolizumab with or without bevacizumab. However, despite these potential advances, there remains an urgent need for novel therapies in the platinum-resistant ovarian cancer space.

One of the very exciting and promising developments over the past few years in ovarian and other cancers has been the evolution of antibody-drug conjugates, or ADCs.

In ovarian cancer, the ADC mirvetuximab soravtansine has provided an early demonstration of the potential promise of these agents. Mirvetuximab is currently FDA-approved for the treatment of folate receptor alpha-high, platinum-resistant ovarian cancer based upon the results of the MIRASOL study, a randomized phase 3 trial which demonstrated that mirvetuximab improved both progression-free and overall survival compared to investigator's choice standard of care chemotherapy. In this trial, mirvetuximab also had a differentiated safety profile from standard chemotherapy with fewer hematologic toxicities but a higher rate of ocular toxicity.

Beyond mirvetuximab, there has been high interest in developing additional ADCs in the ovarian cancer space. In the DESTINY-PanTumor02 basket trial, the HER2-targeting ADC trastuzumab/deruxtecan demonstrated promising early signs of activity in a cohort of 40 ovarian cancer patients whose tumors had HER2 2+ or 3+ IHC by gastric scoring criteria on local testing. Additional ADCs targeting folate receptor alpha are in development, and multiple other targets of interest have emerged, including TROP2, claudin-6, B7-H4, and NaPi2b.

One of the promising targets currently being investigated in the ovarian cancer space is cadherin-6, or CDH6. CDH6 is a transmembrane protein that is embryonically involved in development of the central nervous system circuitry, as well as proximal renal tubules. CDH6 expression has also been reported in the majority of ovarian cancer, with reports varying between 65% to 85% and with expression more frequently observed in high-grade serous ovarian cancers. These characteristics have made CDH6 an attractive potential ADC target in ovarian cancer, and a number of CDH6-targeting ADCs are now in development, including raludotatug deruxtecan, CUSP06, and SIM0505. Well, we're out of time today, but we'll be discussing some of these in the future.

Thank you.

Announcer:
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