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Targeted Therapy in the Treatment of Recurrent Platinum-Resistant Ovarian Cancer

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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Dr. Salani:
This is CME on ReachMD, and I'm Dr. Ritu Salani.

Dr. Colombo:
And I'm Dr. Nicoletta Colombo.

Dr. Salani:
Dr. Colombo, can you take us through the data supporting guideline recommendations for use of targeted therapies in recurrent platinum-resistant ovarian cancer?

Dr. Colombo:
Yeah. Standard chemotherapy provides overall response rate between 10% to 15% and a median progression-free survival of 3.5 months in patients with platinum-resistant ovarian cancer. But the recently published MIRASOL study in patients with platinum-resistant ovarian cancer and a high expression of folate receptor alpha demonstrated that mirvetuximab soravtansine, a folate receptor alpha-directed antibody-drug conjugate, can improve progression-free survival with a hazard ratio 0.65 and overall survival with a hazard ratio of 0.67 compared to standard chemotherapy, consisting in weekly paclitaxel, topotecan, or pegylated liposomal doxorubicin. And response rates increased from 16% with standard therapy to 42% with mirvetuximab.

Another very interesting target is HER2. The DESTINY-PanTumor02 study included 40 patients with ovarian cancer, heavily pretreated with positive expression of HER2, had immunohistochemistry 2+ and 3+. And they were treated with trastuzumab deruxtecan. And the overall response rate was 45% with 11.3 months response duration. Actually, the response rate in the IHC 3+ was 63.6% with a median progression-free survival of 12.5 months. Other interesting ADCs targeting not only folate receptor alpha and HER2, but also other targets such as TROP2, cadherin-6, claudin-6, and B7-H4 are currently under investigation with very promising preliminary activity shown in this population.

Now, Dr. Salani, can you talk about how these clinical data inform current NCCN Guidelines?

Dr. Salani:
Yeah. Thank you for that great summary. And based on the data that you shared, mirvetuximab now has a Category 1 for tumors that express folate receptor alpha 75% or higher, and that's based on the phase 3 data that you shared.

And I think the other area of excitement is trastuzumab deruxtecan. Now this does have NCCN Guideline approval for IHC 2+ and 3+ for HER2 expression; however, the FDA approval is 3+. But I think this is an area of high need. And platinum-resistant ovarian cancer has limited survival, so therapies that have compelling responses are really exciting.

You mentioned other areas that are in exploration. And I also want to highlight that there are other targets for immunotherapy, such as tumor mutational burden-high or mismatch repair deficient, that have pan tumor-agnostic approvals and can be used in ovarian cancer and may be seen in other histologic types, such as clear cell or endometroid cell types, which also may be an avenue of treatment. But it's a really exciting area, and I can't say enough about enrollment in clinical trials so we can continue to improve the lives of these patients.

Dr. Colombo:
Yeah. Thank you, Dr. Salani.

So I think, to summarize, we are finally moving towards a more personalized therapy in platinum-resistant ovarian cancer with biomarker-selected therapies which hold the promise of a substantial improvement in the outcome of this very unfavorable population. Response rates in the range of 45% and 46%, as the one seen with mirvetuximab and trastuzumab deruxtecan, are unprecedented in patients with platinum-resistant ovarian cancer and, I think, represent a substantial step forward in the treatment of these patients.

Dr. Salani:
Yeah, I exactly echo what you just said. And I think it's important to recognize that the prevalence of ovarian cancer is increasing, so the amount of time and the number of women surviving with this disease is increasing. Finding better therapies that are more personalized, directed towards their treatment, and ideally minimizing toxicities is really key for these patients.

Well, that's all the time we have today. Thank you for a great discussion, Dr. Colombo, and thanks to our audience for listening.

Announcer:
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