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First-Line Maintenance Therapy Using PARP Inhibitors for Ovarian Cancer

Announcer:

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Dr. Colombo:

This is CME on ReachMD, and I'm Dr. Nicoletta Colombo.

Dr. Salani:

And I'm Dr. Ritu Salani.

Dr. Colombo:

Dr. Salani, what clinical data support the guidelines for the use of PARP inhibitors as first-line maintenance therapy for ovarian cancer?

Dr. Salani

Yeah, that's a great question and thank you. PARP inhibitors have really revolutionized the management of ovarian cancer patients, particularly in the frontline maintenance setting. So after primary chemotherapy with carboplatin and paclitaxel as the most common regimen, there are some data that shows that the use of PARP inhibitors as a maintenance strategy is advantageous from a survival standpoint.

The most compelling data is in the BRCA mutation carriers, whether it's in their germline or in somatic testing. And we have data from SOLO1 using olaparib in this patient, and that's probably the most long-term data we have. We also have PRIMA using niraparib in this setting. And both of these studies use BRCA mutation carriers and showed a profound benefit with the use of PARP inhibitors.

There are also other studies that have evaluated this. This includes combinations of bevacizumab and PARP inhibitors with olaparib. And we also saw a benefit in this case, PAOLA-1, in those patients who had HRD positivity with the combination of olaparib and bevacizumab compared to bevacizumab alone.

There are other studies exploring this, but I think those 3 have really set the landscape for this patient population in the frontline maintenance therapy. All BRCA mutation carriers should receive it. HRD positivity also derive benefit. And I think that patients who have HRD test negative or BRCA wild-type also may have benefit from it, but we need better strategies in that population.

So, Dr. Colombo, can you talk about how these data inform the current NCCN Guidelines?

Dr. Colombo:

Oh, thank you for asking. So if you look at the current NCCN Guidelines and focus on Category 1 recommendations for first-line maintenance therapy for ovarian cancer, you will see they are based on these main factors: the use of bevacizumab together with chemotherapy in frontline, the presence of a BRCA mutation or homologous recombination deficiency, and the response to chemotherapy. So based on these factors, patients with germline or somatic BRCA mutations who achieve a complete or partial





remission should receive olaparib or niraparib as maintenance.

And patients with homologous recombination deficiency who achieve a complete or partial remission after first-line chemotherapy, which includes bevacizumab, should add olaparib to bevacizumab as maintenance, with the option of substituting olaparib with niraparib if the patient is not able to tolerate olaparib.

Now, the combination of olaparib and bevacizumab is also Category 1 recommendation for patients with BRCA mutation who achieve a complete or partial remission after first-line chemotherapy, which includes bevacizumab. For these patients, there is also the option to stop bevacizumab and continue with a PARP inhibitor alone, such as olaparib, niraparib, or rucaparib, although this is not Category 1 recommendation.

Dr. Salani:

That's a great overview. And just kind of in summary, PARP inhibitors have really kind of changed the survival outcomes for patients with BRCA mutations and those with HRD positivity, but I think we need better strategies in those who are HRD test negative.

Dr. Colombo:

Yeah, I think we can summarize that PARP inhibitors play really a major role in the frontline maintenance treatment of patients with ovarian cancer and play a role in patients with BRCA mutation and/or HRD-positive tumors, I think, is very well established and very consistent across different trials, with unprecedented improvement in progression-free survival in all of them.

Moreover, I think the improvement in overall survival, observed in SOLO1 and PAOLA-1, raises the hope of a potential cure for some patients. And the benefit of adding bevacizumab to PARP inhibitor is still a matter of debate while the benefit of PARP inhibitors in the HRD-negative population is still unclear to me.

This has been a brief but great discussion. I hope we gave you something to think about, and thanks for tuning in.

Announcer:

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