Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting: https://reachmd.com/programs/cme/emerging-and-practice-changing-directions-in-gynecologic-malignances-involving-combination-therapies-with-immune-checkpoint-inhibitors/29753/

Released: 12/20/2024
Valid until: 12/20/2025
Time needed to complete: 1h 03m

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Emerging and Practice-Changing Directions in Gynecologic Malignances Involving Combination Therapies With Immune Checkpoint Inhibitors

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

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Campos:
This is CME on ReachMD, and I'm Dr. Susanna Campos. Today, I'd like to provide an overview of emerging practice-changing directions in gynecological malignancies involving combination therapies with ICIs, immune checkpoints, or PARP inhibitors.

Over the course of the last several years there have been some very pivotal trials that I'd like to share with you in different disciplines. One such trial is the KEYNOTE-A18 study. In cervical cancer there have been numerous landmarks over the course of decades, but I think this is a landmark study. This was a well-orchestrated phase 3 study in patients that were FIGO stages 2014 stages IB2 to IIB, these were node-positive disease, FIGO 2014 stages III to IV, either having node-positive or node-negative disease. They had to have measurable or nonmeasurable disease, and then they were randomized to either cisplatin plus radiation therapy plus pembrolizumab followed by pembrolizumab, or the standard of care: cisplatin plus external beam radiation therapy followed by placebo. It's important to know that this particular study had 2 primary endpoints, both progression-free survival as well as overall survival.

When this study was reported, and the updated progression-free survival at the interim analysis, what we saw was the progression-free survival benefit in favor of the pembro-containing arm. The hazard ratio was 0.68. So this is quite monumental.

Interestingly, when a protocol-specified subgroup analysis was done, the benefit was restricted to that of stages III and IVA. Again, I have to highlight that this is FIGO stage 2014 for the positive nodes. So the FDA reviewed and approved this combination for patients with locally advanced cervical cancer with stages III to IVA FIGO stage 2014.

But this really has changed the management of patients with locally advanced cervical cancer. If a patient has a FIGO stage 2014 stages III to IV, the recommendation is pembrolizumab, cisplatin, and radiation therapy. So another landmark in the management of patients with cervical cancer.

Now, not to be outdone, and pertaining now to ovarian cancer and the role of PARP inhibitors, was a very well-orchestrated trial, the GOG-3025, and this is called the DUO-O study. This is a little bit more of a complicated study. These were patients with newly diagnosed FIGO stage III to IV high-grade epithelial ovarian cancer. They could not have seen prior systemic therapy. They had to be naïve to PARP inhibitors, primary debulking or planned interval debulking surgery, or had to be planned. These patients were randomized to 3 cohorts. One of them, arm A, was carboplatin and paclitaxel plus bevacizumab plus a durvalumab placebo, followed by a maintenance phase of bevacizumab, durvalumab placebo, and olaparib placebo. The second arm was chemotherapy plus bevacizumab plus durvalumab, followed with a maintenance therapy of bevacizumab, durvalumab, and olaparib as a placebo. And the

third arm was an all-comers arm, and that was chemotherapy, bevacizumab, durvalumab, followed in maintenance therapy by bevacizumab, durvalumab, and olaparib.

It's important to note that the primary endpoint of the DUO-O study was the progression-free survival, and they compared arm 3 vs arm 1. So also important to know the eligibility criteria. These were patients that were non-BRCA mutation carriers.

Now, the results of this particular study were updated recently and the final progression-free survival was actually presented. And the final progression-free survival was reported for both the non-BRCA but HRD-positive cohort and the non-BRCA intent-to-treat cohort. And if you take a look at the HRD-positive cohort – again, these are non-BRCA mutation carriers – the median progression-free survival was actually quite robust. It was 45.1 months in arm 3 vs that of 23.3. And this was statistically significant, and the hazard ratio was 0.46.

In a similar light, but perhaps not as robust, with the non-BRCA mutation intent-to-treat population, we're looking at a median progression-free survival of 25.1 months in arm 3 vs that in arm 1, which is just the basic chemotherapy of 19.3. The hazard ratio in this case was 0.61.

This data is quite inviting. We're still trying to place where this can land in the management of ovarian cancer patients.

Well, my time is up. I hope you found this overview useful and thank you for listening.

Announcer:
You have been listening to CME on ReachMD. This activity is provided by Prova Education. and is part of our MinuteCE curriculum.

To receive your free CME credit, or to download this activity, go to ReachMD.com/Prova. Thank you for listening.