Meeting Report

ASCO 2019 meeting review

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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The American Society of Clinical Oncology (ASCO) held its annual meeting in Chicago, USA, on May 31 through June 4, 2019. Throughout the meeting there were several impactful sessions on gynecologic cancers, culminating in the oral abstracts in Gynecologic Oncology, which were heard on Monday June 3rd. This riveting session included report on many influential clinical trials in endometrial, cervical, and ovarian cancer. Key themes at this meeting were in the use of poly (ADP-ribose) polymerase (PARP) inhibitors for ovarian cancer and immunotherapy for endometrial cancer.

Much of the attention in ovarian cancer remains on PARP inhibitors, with 3 oral abstracts presented on use of these agents. First Dr. Mirza et al. [1] presented the results of AVANOVA2, designed to determine if the combination of an anti-angiogenic agent, bevacizumab, can increase progression free survival (PFS) in combination with niraparib in women with platinum-sensitive recurrent ovarian cancer compared with niraparib alone. In total, 97 women were randomized to the combination arm vs. niraparib alone in this chemotherapy-free trial. PFS was improved in the niraparib and bevacizumab arm, with a hazard ratio of 0.35 (95% confidence interval=0.21–0.57), with a 6.4 months improvement in median PFS from 5.5 to 11.9 months. Notably, this benefit was maintained in both the *BRCA* mutated (14.4 vs. 9.0 months) and in the *BRCA* wildtype tumors (11.3 vs. 4.2 months). Hypertension, deep vein thrombosis, and proteinuria were higher as anticipated in the combination arm, however treatment discontinuation for toxicity was low in both arms (13% in combination vs. 10% in niraparib arm), and there was no detriment to quality of life noted with the 2 drug regimen. This successful non-chemotherapy treatment option for women with platinum-sensitive cancer was lauded, and the AVATAR trial randomizing niraparib and bevacizumab vs. standard of care chemotherapy is much anticipated.

Olaparib as treatment was compared to non-platinum chemotherapy in both platinum sensitive (SOLO3) and platinum resistant (CLIO) ovarian cancer. SOLO3, presented by Dr. Penson et al. [2], randomized women with germline *BRCA* mutation with platinum sensitive recurrent ovarian cancer and at least 2 prior lines of therapy to olaparib vs. single agent non-platinum agent chemotherapy. This study met its primary endpoint of overall response rate (ORR) in patients with measurable disease, with 72% in the olaparib arm vs. 51% in the chemotherapy arm, with a median PFS difference of 13.4 vs. 9.2 months. While this study met its primary endpoint, it was criticized in discussion for the absence of platinum chemotherapy for women with platinum-sensitive ovarian cancer.

CLIO utilized the same design, a randomized controlled trial of olaparib vs. non-platinum chemotherapy, in women with platinum-resistant ovarian cancer not selected by *BRCA* status [3]. ORR was not statistically different between the groups ($p=0.13$). In women with *BRCA* mutations, ORR was 36% in the olaparib group vs. 0% in the chemotherapy group, while in contrast in the *BRCA* wildtype group ORR was 13% vs. 6%. Taken together, these trials help solidify the role of olaparib as a treatment option both for women with platinum-resistant ovarian cancer and *BRCA*-mutated tumors in platinum-resistant disease.

In endometrial cancer, the focus was on immunotherapy using checkpoint inhibitors. The importance of mismatch repair (MMR) proficiency was clear, with both large clinical trials presents dividing into MMR deficient and proficient cohorts for study. First, the PHAEDRA study of durvalumab, an anti-programmed death ligand 1 (PD-L1) agent, in advanced or recurrent endometrial cancer was presented by Antill et al. [4]. In this phase II trial, 70 women with measureable disease, 30 in each cohort as defined by immunohistochemistry (IHC), received durvalumab until progression of disease or toxicity. ORR was 43% in the deficient MMR cohort and 3% in the MMR proficient group. Notably, the disease control rate at 16 weeks was 66% in the deficient MMR group and 20% in the proficient MMR group. Further data is awaited from this trial, including biomarker analysis such as PD-L1 staining and translational outcomes from collected tissue to characterize and define the women with endometrial cancer most likely to respond to durvalumab.

A similar phase II study using another PD-L1 inhibitor, avelumab, was presented by Dr. Konstantinopoulos et al. [5]. This trial also included MMR deficient and proficient cohorts in a 2 stage design. Women with recurrent or persistent endometrial cancer were given avelumab until progression or toxicity. Results were similar to PHAEDRA, with improved responses in the MMR deficient tumors. The deficient MMR group of 15 women had a 26.7% ORR with a median PFS of 4.4 months, while the proficient MMR group of 16 patients had only 1 partial response (ORR=6.3%; median PFS=1.9 months), though this patient was still on treatment more than 2 years later. Neither of these immunotherapy trials had new or unexpected safety signals. Interestingly in the avelumab trial the authors investigated 3 methods of determining MMR status, IHC, polymerase chain reaction, next generation sequencing, and the relationship of these results to response. Response rates generally correlated with results in all 3 testing modalities, ranging from 22% to 30% in the deficient group and 6% to 12.5% in the proficient tumors. PD-L1 staining by IHC was not correlated with MMR status, and all objective responses were seen in the PD-L1 negative group. These results highlight the importance of continued biomarker research to enhance our ability to choose the optimal treatment for each patient.

Overall, ASCO 2019 was rich with new data with which oncologists are armed to better treat women with gynecologic malignancies. The importance of research on biomarkers to choose targeted therapy, immunotherapy, and combination therapy was at the forefront, and these themes were echoed in the excellent speaker distillations and educational sessions. In addition, the opportunity for international collaboration and idea generation are a key aspect of this large and important conference, certainly leading to the next wave of research with results anxiously awaited at future meetings.

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