

IN THE NEWS: Updates for Clinicians

OlympiA Study Shows Addition of Olaparib to Standard Therapy Improves Outcomes in Women With High-Risk, HER2-Negative Early Breast Cancer and Inherited Mutations in *BRCA1* or *BRCA2* Genes (continued from page 2)

Invasive disease-free survival (IDFS, the primary endpoint) was significantly improved with olaparib vs. placebo (three-year IDFS 85.9% vs. 77.1%, $P < 0.0001$). Similarly, three-year distant disease-free survival (DDFS) was significantly improved with olaparib vs. placebo (87.5% vs. 80.4%; $P < 0.0001$). Though fewer deaths were reported with olaparib, the overall survival benefit was not significant, with a short follow-up period of only two and a half years.

Side effects were consistent with those seen with olaparib in prior studies (nausea and vomiting, fatigue and anemia) and were limited and manageable without an effect on patient-reported quality of life. Follow-up will continue for up to 10 years.

References

1. Tutt A, et al. *J Clin Oncol*. 2021;39(suppl 15; Abstr LBA1).
2. Tutt A, et al. *N Engl J Med*. 2021. DOI: 10.1056/NEJMoa2105215.



Expert Commentary

By: Cheryl Jones, MD

This is a practice-changing study that has already been endorsed by ASCO to adopt the use of the PARPi, olaparib, in eligible patients with germline *BRCA*-mutations and HER2-nonamplified tumors. Although this study applies to only 5-10% of all breast cancer patients, it highlights what a more nuanced understanding of oncogenic biology has made possible. This understanding

has significantly improved outcomes through the corresponding development of targeted therapies with manageable side effects. The Northside Hospital Cancer Institute participated and enrolled patients in this trial, which underscores the importance of providing access to cutting edge research for community oncologists and their patients.

Immunotherapy Significantly Improves Disease-Free Survival After Surgery in Patients With High-Risk Clear Cell Renal Cell Carcinoma (RCC): Results of the KEYNOTE-564 Study

Findings from a phase 3 study presented at the 2021 Annual Meeting of the American Society of Clinical Oncologists demonstrated that patients who received IV pembrolizumab immunotherapy after nephrectomy for kidney cancer had improved survival compared to patients who did not receive adjuvant pembrolizumab. Kidney cancer, RCC, accounts for approximately 5% and 3% of all new cancers in males and females, respectively. Removal of all the kidney or part of the kidney, radical or partial nephrectomy, has been the standard of care treatment for locoregional RCC, yet nearly half of patients eventually experience disease recurrence after surgery.

KEYNOTE-564, a phase 3 multicenter trial, randomized 994 patients with clear cell RCC to (approximately one year of) pembrolizumab vs. placebo (observation only) following nephrectomy. Disease-free survival, the primary endpoint of the study, was significantly improved in patients that received pembrolizumab vs. placebo (24-month DFS 77.3% vs. 68.1%, $P = 0.001$). This benefit was consistent across all subgroups analyzed, including those patients with no evidence of disease after resection, but who are at high-risk of relapse. KEYNOTE-564 is the first positive phase 3 study of an adjuvant immunotherapy in RCC.

Reference

- Choueiri TK, et al. *J Clin Oncol*. 2021;39(suppl 15; Abstr LBA5).



Expert Commentary

By: Daniel Canter, MD

Since the approval of tyrosine-kinase inhibitors (TKIs) for the treatment of advanced kidney cancer in 2006, there had been no adjuvant trial demonstrating a survival advantage for patients after surgery, even in patients who were considered high risk for disease recurrence. These prior negative studies were disappointing considering how much TKIs, and now systemic immunotherapy, have improved survival in patients with recurrent or de novo metastatic RCC. With the recent findings from KEYNOTE-564, patients with RCC who have a high risk of recurrence may have an available therapy that appears

to significantly reduce the chance of disease recurrence when compared to the current standard of care, which is radiologic observation. Nevertheless, it is important to point out that this study only reported disease-free survival at 24 months, but the presumption is that in longer term follow-up, patients receiving pembrolizumab will have a better overall survival compared to the placebo group. If, in fact, these results bear out, this data would transform the standard of care for patients who have a high risk of recurrence after definitive surgery.