

# ASCO 2018: Less is more as ‘tailoring’ takes on new meaning

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A record-setting 40,000-plus oncology professionals attended this year’s annual meeting of the American Society of Clinical Oncology (ASCO) in Chicago. The outstanding education and scientific program, with the theme of *Delivering Discoveries: Expanding the Reach of Precision Medicine*, was planned and led by ASCO President Dr Bruce Johnson, professor and director of Thoracic Oncology at the Dana Farber Cancer Institute in Boston, and chaired by Sarah Cannon’s Dr David Spigel and Harvard’s Dr Ann Partridge. A recurring finding throughout the meeting was that “less is more” in several key areas of cancer therapy. From small molecules targeting driver mutations across various tumors to the application of immunotherapy in subsets of common cancers, it is clear that more patients are experiencing dramatic results from novel approaches.

A featured plenary session trial was TAILORx, a study of 10,273 women with hormone-receptor-positive, surgically resected breast cancer that had not spread to the lymph nodes, was less than 5 cm, and was not positive for the HER2 gene amplification. This clinical trial was sponsored by the NCI and initiated in 2006. It used the OncotypeDX genetic test to stratify patients into groups of low, intermediate, or high risk for recurrence. The low-risk patients received only hormonal therapy, and the high-risk patients were treated with hormonal therapy plus chemotherapy.

Dr Joseph Sparano, professor of Medicine and Women’s Health at the Albert Einstein College of Medicine in New York, presented the results from the group of 6,700 intermediate risk women who were randomized to receive hormonal therapy alone or in combination with chemotherapy. After 9 years of follow-up, 83.3% of the volunteers, as Dr Sparano appropriately referred to them, who were treated with hormonal therapy were still cancer free, compared with 84.3% of those who also received chemotherapy, demonstrating no statistical benefit for the addition of chemotherapy. Of note, breast cancer experts discussing the trial, including Dr Lisa Carey, professor of Breast



Cancer Research at the UNC Lineberger Cancer Institute in Chapel Hill, urged that younger women, under the age of 50, with recurrence scores (RS) toward the higher end of the intermediate risk group (RS, 16-25) should still discuss and consider chemotherapy with their physicians. In summary, all patients fitting the study criteria with low (<11) and lower intermediate (<16) RS can avoid chemotherapy, as well as those patients over the age of 50 with RS <26.

These landmark and practice changing results mean that each year about 60,000 women in the United States will be spared the side effects of toxic drugs. These 10,273 study volunteers are true heroes to the women who will be diagnosed with breast cancer in coming years.

In the field of lung cancer, many new trial results using immunotherapy were presented, with the most talked about being single-agent pembrolizumab, a PD1 inhibitor, improving survival over traditional chemotherapy in patients with PD-L1 positive tumors, which comprise the majority of squamous cell and adenocarcinomas of the lung. Also in the plenary, Dr Gilberto Lopes of the Sylvester Cancer Center at the University of Miami, presented these results from the KEYNOTE-042 study. In patients with PD-L1 tumor proportion score (TPS) of >1%, the benefit in overall survival (OS) of pembrolizumab compared with chemotherapy was 16.7 versus 12.1 months, respectively (HR, 0.81). In those patients with a TPS of >20%, the OS benefit was 17.7 versus 1.0 months (HR, 0.77), and in the group with a TPS of >50%, the benefit was 20.0 versus 12.2 months (HR, 0.69). Overall, the quality of life and the occurrence of side effects were substantially better for those patients receiving immunotherapy alone. Other findings presented at the meeting demonstrated the benefit of adding immunotherapy to chemotherapy and of treating with combination immunotherapy (PD-1 and CTLA-4 inhibitors). Many options now exist, much work remains to be done, and accrual to clinical trials is more important than ever.

Another plenary session trial evaluated the benefit of per-

forming a nephrectomy in patients with advanced or metastatic renal cell carcinoma (RCC), a long-held and practiced standard of care. Dr Arnaud Mejean of Paris Descartes University presented findings from the CARMENA trial, which randomized 450 patients with metastatic clear cell RCC to receive cytoreductive nephrectomy followed by sunitinib, or sunitinib alone. The OS results of 18.4 versus 13.9 months, respectively (HR, 0.89) favored sunitinib alone in this noninferiority analysis. Other endpoints lined up in favor of not removing the cancerous kidney, and the presenter and discussants were united in their opinion of the results and the resulting change in doing less surgery in these patients.

In a step away from less therapy, the European Pediatric Soft Tissue Sarcoma Study showed that adding 6 months of low-dose maintenance chemotherapy after standard intensive therapy improves survival in children with high-risk rhabdomyosarcoma. The addition of a vinorelbine and cyclophosphamide low-dose regimen improved 5-year disease-free survival from 69.8% to 77.6% (HR, 0.68) and OS from 73.7% to 86.5% (HR, 0.52) as presented by Dr Gianni Bisogno, University of Padovani, Italy. The mainte-

nance regimen showed no increase in toxicity and actually fewer infections were noted.

In the area of molecular profiling, multiple studies at the meeting demonstrated the importance of assessing cancers for mutations as outstanding results were seen with therapies for NTRK, RET, ROS, and MSI-high driven tumors. In a debate on the role of molecular profiling, I had the opportunity to declare and support our position at Sarah Cannon that all patients with relapsed or metastatic cancers should have this testing performed. It will be through better understanding of the biology of these cancers that we will advance the field for all patients while sometimes finding a target or mutation that will dramatically change the life of a patient.

In keeping with the meeting's theme, *Delivering Discoveries: Expanding the Reach of Precision Medicine*, the presentations and the discussions clearly demonstrated that through the use of precision medicine techniques such as prognostic gene assays and molecular profiling, patients can receive the best therapy, even "tailored" therapy, which may often actually be less therapy. It is an exciting time in cancer research, and I have never been more optimistic about the future of cancer treatment for our patients.