Adding Immunotherapy to Standard Treatment Slows Growth of Advanced Kidney Cancer, With Fewer Side Effects

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Contact
Ashley Yum
571-483-1376
ashley.yum@asco.org

Expert Perspective

“Adding immunotherapy to existing targeted therapies has shown promising results in recent clinical trials. We’re pleased to see validation of this approach through this large trial in advanced kidney cancer, a disease that remains incurable for most patients,” said ASCO Expert Sumanta K. Pal, MD, moderator of today’s presscast.

ALEXANDRIA, Va. – In a phase III clinical trial of people with previously untreated metastatic renal cell cancer (mRCC), combining immunotherapy atezolizumab with targeted therapy bevacizumab delayed cancer growth by about three months longer than sunitinib, another targeted therapy. The benefit of atezolizumab plus bevacizumab was greater for patients with PD-L1-positive tumors. These findings will be presented at the upcoming 2018 Genitourinary Cancers Symposium in San Francisco, California.

“The side effects of atezolizumab plus bevacizumab were decidedly less harsh than sunitinib. And because progression-free survival was also better, I am confident that this relatively easy-to-administer combination will be a strong treatment choice in all medical practices,” said lead study author Robert J. Motzer, MD, a medical oncologist at Memorial Sloan Kettering Cancer Center, New York.
About the Study

It is estimated there will be 65,340 new cases and 14,970 deaths from kidney and renal pelvic cancers in the United States in 2018. Renal cell cancer is the most common type of kidney cancer in adults. IMmotion151 is the first randomized, phase III combined immunotherapy with bevacizumab trial in people with untreated mRCC. Starting in 2015, sites worldwide enrolled 915 adults who were randomly assigned to receive either atezolizumab plus bevacizumab intravenously every 3 weeks or take a sunitinib pill daily for 4 weeks followed by two weeks off treatment.

Atezolizumab is an immune checkpoint inhibitor that blocks the PD-L1 protein on the surface of tumor cells, allowing the immune system to recognize and attack those cells. Bevacizumab and sunitinib are targeted medicines that block the growth of blood vessels to the tumor, thereby limiting its growth.

“With the introduction of checkpoint inhibitors, clinicians started looking at combinations of these medicines with anti-angiogenic medicines like bevacizumab,” said Dr. Motzer. “Bevacizumab may affect the local immune response in the tumor and help prime the response of tumor and immune cells to immune-system activators like atezolizumab.”

Key Findings

For the analysis, the researchers grouped patients according to PD-L1 expression on immune cells in the tumor (so-called tumor infiltrating immune cells). Tumors that had the PD-L1 protein detected on the surface of at least 1% of those immune cells were considered PD-L1-positive, and all other tumors were considered PD-L1-negative.

The study had co-primary endpoints:

- Investigator-assessed progression-free survival in the PD-L1-positive group
- Overall survival in the group of all enrollees, also called the intention-to-treat (ITT) population

At a median follow-up of 15 months, patients in the PD-L1-positive group treated with atezolizumab and bevacizumab had a 26% lower chance of the cancer worsening than those who received sunitinib; the median time until the cancer worsened was also 3.5 months.
longer (median 11.2 months in the atezolizumab plus bevacizumab group vs. 7.7 months in the sunitinib group).

In the ITT group, a benefit of atezolizumab plus bevacizumab was also observed, though more modest. Those treated with atezolizumab and bevacizumab had a 17% lower chance of cancer worsening, with a median time of 2.4 months longer until the cancer worsened. The difference in overall survival between the two treatment regimens was not statistically significant at this early interim analysis. Overall survival data are still immature, and the authors are planning an updated analysis as more data accrues.

Treatment-related side effects were less frequent in the atezolizumab and bevacizumab group, occurring in 40% of people, compared to 54% of people in the sunitinib group. Twelve percent of people in the atezolizumab and bevacizumab group, and 8% in the sunitinib group, stopped at least one treatment component due to treatment-related side effects during the trial.

“For an aggressive cancer like this, where less than 20% of people survive 5 years after diagnosis, we think a 3.5 month longer progression-free survival, given the tolerability for this new combination treatment regimen, is an important development,” said Dr. Motzer.

**Next Steps**

The study will continue to assess overall survival as specified by protocol as well as secondary endpoints. In addition, the researchers collected tumor tissue and will look at molecular profiles to try to tease out markers, in addition to PD-L1, in the people who responded best to the combination therapy. Dr. Motzer said the researchers may look at novel therapies that could be added to atezolizumab so they could devise treatments to boost survival odds even higher.

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View the full abstract.

For your readers:
• Guide to Kidney Cancer
• Understanding Immunotherapy

2018 Genitourinary Cancers Symposium News Planning Team:
Sumanta K. Pal, MD, American Society of Clinical Oncology (ASCO); Daniel A. Hamstra, MD, PhD, American Society for Radiation Oncology (ASTRO); and Katie Murray, DO, Society of Urologic Oncology (SUO)

View the disclosures for the News Planning Team.

ATTRIBUTION TO THE 2018 GENITOURINARY CANCERS SYMPOSIUM IS REQUESTED IN ALL NEWS COVERAGE.

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About the American Society for Radiation Oncology:
The American Society for Radiation Oncology (ASTRO) is the world’s largest radiation oncology society, with more than 10,000 members who are physicians, nurses, biologists, physicists, radiation therapists, dosimetrists and other health care professionals who specialize in treating patients with radiation therapies. The Society is dedicated to improving patient care through professional education and training, support for clinical practice and health policy standards, advancement of science and research, and advocacy. ASTRO publishes three peer-reviewed journals, the International Journal of Radiation Oncology • Biology • Physics (redjournal.org), Practical Radiation Oncology (practicalradonc.org) and Advances in Radiation Oncology (advancesradonc.org); developed and maintains an extensive patient website, RT Answers (ranswers.org); and created the Radiation Oncology Institute (roinstitute.org), a nonprofit foundation to support research and education efforts around the world that enhance and confirm the critical role of radiation therapy in improving cancer treatment. To learn more about ASTRO, visit www.astro.org, sign up to receive our news and follow us on our blog, Facebook and Twitter.

About ASCO:

Founded in 1964, the American Society of Clinical Oncology, Inc. (ASCO®) is committed to making a world of difference in cancer care. As the world's leading organization of its kind,
ASCO represents more than 40,000 oncology professionals who care for people living with cancer. Through research, education, and promotion of the highest-quality patient care, ASCO works to conquer cancer and create a world where cancer is prevented or cured, and every survivor is healthy. ASCO is supported by its affiliate organization, the Conquer Cancer Foundation. Learn more at www.ASCO.org, explore patient education resources at www.Cancer.Net, and follow us on Facebook, Twitter, LinkedIn, and YouTube.

**About the Society of Urologic Oncology:**

The Society of Urologic Oncology (SUO) was created in 1984 to enable qualified members primarily interested in the care of patients with malignant genitourinary diseases to meet for the purpose of discussion, development, and implementation of ideas to improve care. The Society and its bylaws conform to the guidelines and bylaws of the American Urological Association (AUA).

The purpose of the SUO is to develop educational and research initiatives and to study issues in urologic oncology and provide physician statements that represent a state of the art assessment of these issues to other organizations.

The Society also provides a forum for identifying the urologic oncologist as a physician with specific expertise in the study and treatment of genitourinary malignancies. In recognition of the multidisciplinary efforts involved in the study and treatment of genitourinary malignancies, the Society seeks to incorporate multiple disciplines in achieving these goals. The Society supports the activities of multiple disciplines in the common objectives of seeking an increased understanding and successful treatment of genitourinary malignancies.

The SUO seeks to improve the care of patients with malignant urologic disease and to provide a forum for the discussion of problems relating to malignant urologic disease. Our objectives include: 1) Stimulating research in and the teaching of urologic oncology, 2) Disseminating the principles of urologic oncology to the medical profession at large, 3) Bringing urologists into a Society whose work is entirely, or principally with malignant disease, 4) Being identified as the most qualified organization on matters relating to urologic oncology, and 5) Standardize fellowship training in urologic oncology.

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