Pembrolizumab Plus Axitinib Extended Overall Survival and Progression-Free Survival Versus Current Standard Treatment for Advanced Kidney Cancer

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MEDIA CONTACT:
Kelly Baldwin
571-483-1365
kelly.baldwin@asco.org

PATIENT AND CAREGIVER INQUIRIES:
Contact Cancer.Net

Expert Perspective
“Metastatic kidney cancer has very low survival rates and there have been few significant advances in treating this advanced form of the disease. These findings may help provide an important new option for patients,” said ASCO Expert Robert Dreicer, MD, MS, MACP, FASCO, moderator of today’s presscast.

ALEXANDRIA, Va. -Results from the randomized, phase III KEYNOTE-426 clinical trial show that first-line therapy with a combination of the PD-1 targeted immunotherapy pembrolizumab (Keytruda) and the VEGF-targeted tyrosine kinase inhibitor axitinib (Inlyta) extended both overall survival and progression-free survival for patients with clear-cell metastatic renal cell carcinoma (mRCC), compared with the current standard of care, sunitinib (Sutent). Findings from this international study will be presented at the upcoming 2019 Genitourinary Cancers Symposium in San Francisco, California.

“These results are exciting,” said co-lead study author Thomas Powles, MD, Professor of Urology Oncology at Barts Cancer Institute in London, England. “By adding pembrolizumab to a VEGF-targeted therapy, we are seeing powerful anticancer responses, including improved survival – and importantly, the results are seen across broad subgroups of patients.”
Pembrolizumab is an immune checkpoint inhibitor that blocks the PD-1 protein on the surface of immune cells, which allows the immune system to then recognize and attack tumor cells. Axitinib and sunitinib are antiangiogenic medicines that can block the growth of blood vessels to the tumor, therefore limiting its growth.

It is estimated there will be 73,820 new cases and 14,770 deaths from kidney cancer in the United States in 2019, about 95% of which result from renal cell cancers. Metastatic RCC has a 5-year survival rate of 12%.

**About the Study**

In the study, 861 people with untreated clear-cell mRCC were randomly assigned to oral sunitinib once daily or to combination therapy, with pembrolizumab given intravenously every 3 weeks along with oral axitinib twice daily. Treatment continued until the disease progressed, patients developed high toxicity, or they dropped out of the study. The median patient age in the trial was 62, and 73% of the participants were male and 27% were female.

These results build on findings from an earlier phase Ib trial, which found pembrolizumab plus axitinib had a manageable safety profile and a high response rate (73%) among patients with mRCC. Following these positive results, investigators proceeded directly to this phase III trial.

“Both pembrolizumab and axitinib have shown efficacy against mRCC on their own,” said Dr. Powles. “Antiangiogenic therapy such as axitinib facilitates immune T-cell infiltration.” According to Dr. Powles, phase Ib study results indicated that axitinib was easier to combine with pembrolizumab than some other antiangiogenic drugs in the same class as sunitinib.

**Key Findings**

At a median follow-up of 12.8 months, a comparison of patients receiving combination therapy vs. sunitinib showed that:

- **Overall survival**: Combination therapy was associated with a 47% reduction in the risk of death compared with sunitinib (HR: 0.53); the 12-month overall survival rate was 89.9% in the combination group vs 78.3% in the sunitinib group. These benefits were seen irrespective of risk group or PD-L1 status.
- **Progression-free survival**: With the combination patients lived a median of 15.1 months without disease progression vs. 11.1 months with sunitinib.
- **Overall response rate**: 59.3% with the combination vs. 35.7% with sunitinib.
- **Duration of response**: Longer in patients treated with combination therapy, with a median not yet reached vs. 15.2 months with sunitinib.
- **Ongoing treatment**: With the combination 59.0% of patients continue to be treated vs. 43.1% with sunitinib.
Serious treatment-related side effects were seen in 62.9% of people on the combination therapy compared to 58.1% who received sunitinib. These side effects led to discontinuation of all treatment in 8.2% vs. 10.1% of the groups, respectively.

**Next Steps**

“We have a number of unanswered questions at this point, particularly the absence of biomarkers to predict response. PD-L1 levels, which have been markers for immunotherapy success in other cancers, remain unproven in renal cancer. It is possible that by combining pembrolizumab with axitinib, the predictive value of PD-L1 is being masked,” said Dr. Powles. “Overall, we have not previously seen a renal cancer study which has improved response, progression-free survival, and overall survival. This is therefore a major step forward in renal cancer.”

This study was funded by Merck Sharp & Dohme.


**View the full abstract.**

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- Guide to Kidney Cancer
- Understanding Immunotherapy
- Understanding Targeted Therapy

**2019 Genitourinary Cancers Symposium News Planning Team:**
Robert Dreicer, MD, MS, MACP, FASCO, 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.

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**About the American Society for Radiation Oncology:**
The American Society for Radiation Oncology (ASTRO) is the premier radiation oncology society in the world, with more than 10,000 members who are physicians, nurses, biologists, physicists,
radiation therapists, dosimetrists and other health care professionals that specialize in treating patients with radiation therapies. As the leading organization in radiation oncology, 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 medical journals, *International Journal of Radiation Oncology, Biology, Physics*, *Practical Radiation Oncology*, and *Advances in Radiation Oncology*, developed and maintains an extensive patient website and created the Radiation Oncology Institute, a non-profit foundation to support research and education efforts around the world that enhance and confirm the critical role of radiation therapy in improving cancer treatment. Learn more about ASTRO.

**About the American Society of Clinical Oncology:**

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 nearly 45,000 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.

Please visit our website or call (847) 264-5901 for more information on how to become a member.