Many Advanced Kidney Cancer Patients Don’t Need Surgery

Those who received targeted therapy did equally well without kidney removal.

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People with advanced kidney cancer who take Sutent (sunitinib) do not need to undergo nephrectomy, or kidney removal, according to study results presented at the recent American Society of Clinical Oncology annual meeting in Chicago.

Patients who took Sutent and did not have a kidney removed had a median survival of 18.4 months, compared with 13.9 months for those who underwent nephrectomy followed by treatment with Sutent.

“Thanks to this research, many patients with advanced kidney cancer can be spared unnecessary surgery and a host of severe side effects that often accompany it,” said ASCO Expert Sumanta Pal, MD, of City of Hope in Duarte, California.

Renal cell carcinoma (RCC), which originates in the kidney tubules, is the most common type of kidney cancer. About 63,300 people will be diagnosed with kidney cancer and nearly 15,000 people will die from it this year, according to the American Cancer Society.

For the past two decades, complete or partial kidney removal (cytoreductive nephrectomy) has been considered standard therapy for people with metastatic RCC that has spread beyond the kidney. But surgery carries risks, including bleeding, infection and pulmonary embolism (blood clots in the lungs), and can delay the initiation of anticancer medications.

The CARMENA study aimed to reassess the role of nephrectomy in people with metastatic RCC given the availability of targeted therapies like Sutent, a multikinase inhibitor that blocks the activity of tyrosine kinases that play a role in tumor growth and blood vessel formation.

“Our study is the first to question the need for surgery in the era of targeted therapies and clearly shows that surgery for certain people with kidney cancer should no longer be the standard of care,” said lead investigator Arnaud Mejean, MD, of Paris Descartes University.

This Phase III study included 450 people in France, Norway and the United Kingdom who had metastatic clear cell RCC that had already spread beyond the kidney at the time of diagnosis.

Three quarters were men and the median age was 63. About 40 percent were considered to have a poor prognosis while about 60 percent had an intermediate prognosis score; those with a good prognosis were not included. They had received no prior systemic therapy for RCC and were deemed eligible for both surgery and treatment with Sutent.

Participants were randomly assigned either to undergo nephrectomy and then start Sutent after three to six weeks or to receive Sutent immediately without surgery. In both groups, Sutent was given at a dose of 50 milligrams once daily in cycles of four weeks on and two weeks off. Some people assigned to surgery never received it, and some assigned to Sutent alone ended up having surgery later; in both groups some patients never started Sutent.

Mejean presented findings from a planned interim analysis with a median follow-up period of 51 months. At this point, there were 161 deaths in the Sutent-only group and 165 deaths in the nephrectomy plus Sutent group.

The median overall survival was 18.4 months in the Sutent-only group and 13.9 months in the nephrectomy plus Sutent group, showing that Sutent alone was noninferior to the standard of care. Although survival was longer in the first group, the study was not designed to show whether Sutent alone is superior, Mejean said.

Patients with intermediate prognosis scores lived longer than those classified as having a poor prognosis, but in both groups survival was better with Sutent only than with surgery followed by Sutent (23.4 versus 19.0 months for an intermediate prognosis; 13.3 versus 10.2 months for a poor prognosis).

Progression-free survival, meaning patients were still alive without worsening of disease, was also longer in the Sutent-only group (8.3 months) compared with the surgery plus Sutent group (7.2 months).

Objective response rates, meaning complete or partial tumor shrinkage, were 29.1 percent and 27.4 percent, respectively. Disease control rates, meaning either complete or partial response or stable disease, were 74.6 percent and 61.8 percent, respectively. These differences were not statistically significant, suggesting they could be attributable to chance alone. However, the likelihood of clinical benefit—defined as disease control beyond 12 weeks—was significantly greater in the Sutent-only group (47.9 percent versus 36.6 percent).

The safety of Sutent was similar in both groups. More people taking Sutent alone had severe side effects than those who received surgery first (43 percent versus 33 percent), but they took the drug longer (8.5 versus 6.7 months). The most common side effects were weakness, hand-foot syndrome (redness and peeling of the skin on the palms and soles of the feet), anemia and neutropenia.

“Sunitinib alone was not inferior to nephrectomy followed by sunitinib in patients with metastatic renal cell carcinoma who were classified as having intermediate-risk or poor-risk disease,” the researchers concluded.

Based on this interim analysis, the trial was stopped early because it showed that surgery did not improve outcomes. The study was selected for presentation at an ASCO plenary session featuring research deemed to have the greatest potential impact on patient care.

Commenting on the findings after the presentation, Daniel George, MD, of Duke University said that people similar to the CARMENA population with high-volume metastatic kidney cancer should receive systemic therapy such as Sutent first, while those with low-volume metastatic cancer might start with Sutent and consider surgery afterward. Surgery is still recommended for those with Stage I, II or III kidney cancer that has not spread to distant sites in the body.

Considering potential reasons for these results, George suggested that postoperative wound healing and inflammatory responses to surgery might promote tumor growth.

Other systemic therapy options for kidney cancer include another multikinase inhibitor, Cabometyx (cabozantinib), and an immunotherapy combination of Opdivo (nivolumab) plus Yervoy (ipilimumab).

Click here to read the ASCO study abstract.

Click here for the New England Journal of Medicine report on the study.
