Many elderly patients with metastatic renal cell carcinoma benefit from targeted therapies

Many elderly patients with metastatic renal cell carcinoma (RCC)—who are often underrepresented in clinical trials to treat the kidney cancer—are seeing overall survival benefits from treatment with targeted therapies, according to a new study from Penn Medicine researchers published this month in *JAMA Network Open*. Analyzing 13 years of data on Medicare patients, the study found that the patients who received targeted therapies were more medically complex than those who received the older, more toxic treatments that were available earlier in the study period, indicating that newer treatments are offering hope to more people.

Since 2005, the U.S. Food and Drug Administration has approved 12 targeted therapies for the treatment of advanced RCC. However, clinical trials investigating these therapies often exclude sicker patients and those over the age of 65, leaving a gap in knowledge about the effectiveness of newer versus older treatments in this population, especially when they are treated in routine health care settings rather than in research studies.

"Our findings suggest that targeted therapies offered new treatment options to elderly and medically complex patients who may have otherwise foregone the treatments available 15 years ago given their high toxicity and limited benefit," said senior author Jalpa A. Doshi, Ph.D., a professor of Medicine in the Perelman School of Medicine at the University of Pennsylvania. "RCC is a cancer where people can often try other treatment options if the first one isn't effective, so even small gains may mean that a person might live long enough to try the next innovation. What's more, studies are showing that current treatments, including immunotherapies, are leading to even better outcomes than those that were observed during our study time frame."

Results also showed that targeted therapies offered a modest survival benefit as compared to older treatments, even though as a whole, the targeted therapy treatment group had characteristics that put them at risk for worse outcomes.

The researchers conducted a retrospective cohort study using Surveillance, Epidemiology, and End Results (SEER)-Medicare data from 2000 to 2013 to examine overall survival and estimated overall survival improvements in over 1,100 patients with stage IV clear cell RCC who received any FDA-approved targeted therapy (63 percent of patients) or nontargeted therapy (37 percent of patients). Most patients were aged 65 or older, and approximately 13 percent were younger but eligible for Medicare due to disability prior to their RCC diagnosis.

The initial analysis found no statistically significant difference in survival between targeted and
nontargeted therapies. However, a more in-depth analysis that used statistical techniques to mimic the more controlled conditions found in clinical trials—known as an instrumental variable analysis—revealed a three-month survival advantage with targeted therapies compared to older treatments. Estimated overall survival improvements with targeted therapy versus nontargeted therapies were also statistically significant—eight percent at one year, seven percent at two years, and five percent at three years.

"The more sophisticated statistical methods allowed us to see an unbiased picture of how the treatments compared in the real world," said first author Pengxiang Li, Ph.D., a senior research investigator at Penn Medicine. "The method helped control for unmeasured differences between the treatment groups, which cannot be adjusted using traditional approaches."

Despite the findings, the median survival benefits observed in this real-world patient population were smaller compared to the benefits seen in clinical trial participants enrolled in randomized studies of targeted therapies. The combined findings underscore that research studies summarize outcomes for groups of patients and may not accurately reflect how treatments will perform in the real world or what any individual patient can expect from treatment.

For example, in this study, half of the targeted therapy group had passed away within nine months, but 10 percent of people survived longer than 47 months. Among that group with better outcomes, targeted therapies offered an 11-month survival advantage over older treatments, the researchers reported.

"Treatment decisions involve weighing potential risks, benefits, and costs of treatment as well as quality-of-life considerations, which may vary from person to person depending on their medical situation and preferences. Good communication between patients and their treatment teams is essential, and knowing more about real-world outcomes can help with those discussions," said co-author Amy R. Pettit, Ph.D., adjunct fellow at the Penn Center for Public Health Initiatives.