Assessing an Immunotherapy Benefit for Specific Kidney Cancer Patients

A unique analysis measures treatment-free survival after immunotherapy in patients with advanced renal cell carcinoma.

November 22, 2021 By Dana-Farber Cancer Institute

Patients with advanced renal cell carcinoma who received the checkpoint inhibitor combination nivolumab [Opdivo] plus ipilimumab [Yervoy] experienced longer treatment-free survival (TFS) over a 42-month period than patients with that type of kidney cancer who received the targeted therapy sunitinib, regardless of the International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) risk group, according to new analysis of the CheckMate 214 clinical trial published in Clinical Cancer Research, a journal of the American Association for Cancer Research.

TFS, as defined by the study author Meredith Regan, ScD, of Dana-Farber Cancer Institute and an associate professor at Harvard Medical School, is the time between ending the protocol-assigned therapy and starting a subsequent therapy or death, for the entire trial cohort.

“One of the great challenges in conducting clinical trials is that some of the endpoints we’ve been using to measure the efficacy and value of a treatment are not optimal, especially when evaluating immuno-oncology-based therapy regimens,” said Regan.

She and her collaborators recently proposed the new TFS outcome to incorporate the quality of survival time into the trial analysis to better inform clinical decision-making.

“As we continue to develop new treatments, we have an opportunity to think about new methods to better balance the efficacy and toxicity to the patients,” added Regan. “To do that, we needed a new endpoint to quantify those two aspects together—to continue to improve survival for patients while also focusing on how they are spending their time. That’s how TFS came to be.”

The authors are now applying TFS analysis retrospectively to prior clinical trials to complement the standard endpoints, and plan to use the new endpoint prospectively in future trials.

In this study, they evaluated TFS in the CheckMate 214 phase III trial. Results of this trial showed a significantly longer overall survival with the nivolumab and ipilimumab combination (nivolumab + ipilimumab) than with sunitinib in patients receiving their first therapy for advanced renal cell carcinoma with both intermediate and poor prognostic risk and favorable risk, assessed per the

IMDC. At 42 months since initiating therapy, 52 percent and 39 percent of patients were alive with nivolumab + ipilimumab and sunitinib, respectively.

The TFS analysis was performed for the 42-month time period and included all patients (550 who received nivolumab + ipilimumab and 546 who received sunitinib). TFS was subdivided into treatment-free survival with and without toxicity by counting the days in which patients experienced moderate and severe treatment-related adverse events (TRAEs).

According to this analysis, over the 42-month period, the mean TFS was more than twice as long after nivolumab + ipilimumab than sunitinib for patients with intermediate/poor risk (6.9 months and 3.1 months, respectively), and three times as long for patients with favorable risk (11.0 months and 3.7 months, respectively). The mean TFS with severe TRAEs was a small fraction of time for both treatments and both risk groups (0.6 months and 0.3 months after nivolumab + ipilimumab and sunitinib, respectively, for intermediate/poor-risk patients; 0.9 months and 0.3 months after nivolumab + ipilimumab and sunitinib, respectively, for favorable-risk patients).

Notably, while the overall survival was similar with nivolumab + ipilimumab and sunitinib in patients with favorable risk, the TFS analysis revealed a difference in how this time was spent between the two treatments: at 42 months, 20 percent of patients treated with nivolumab + ipilimumab and 9 percent of patients treated with sunitinib were treatment-free. Overall, patients with favorable risk who received sunitinib spent more time on protocol therapy and experienced moderate TRAEs for longer time than their counterparts who received nivolumab + ipilimumab.

“This analysis is very patient-centered, and the implications of this work are that we have a new way to assess the value of new treatments to patients when we do clinical trials,” said Regan. “We knew from the previous CheckMate 214 analysis that nivolumab + ipilimumab improved survival compared with sunitinib; now, we are able to compare the way patients spent that overall survival time on these two different treatment approaches, and I think having this information is an important complement to the original trial results.”

The limitations of this study included that the researchers conducted the TFS analysis retrospectively, so the results had to be interpreted in the context of the existing protocol.

“This is a work in progress as we’re continuing to refine this approach to better define how we evaluate toxicity,” said Regan. “We counted the days when patients experienced adverse events and registered their severity, but that didn’t take into account the type of adverse event or if more than one occurred on the same days.”

Another potential limitation in the application of TFS in future clinical trials is that data collection could become more labor-intensive and costly. Furthermore, continuing to collect data on quality of life in the long run once patients stop the protocol-assigned treatment might be challenging.

The senior author of the study is David F. McDermott, MD, of Beth Israel Deaconess Medical Center, Dana-Farber/Harvard Cancer Center. Co-authors of the study are Opeyemi A. Jegede, MPH, and Charlene M. Mantia, MD, both of Dana-Farber; Thomas Powles, MBBS, of Barts Cancer

Institute; Lillian Werner, MS, of Dana-Farber; Robert J. Motzer, MD, of Memorial Sloan Kettering Cancer Center; Nizar M. Tannir, MD, of University of Texas MD Anderson Cancer Center; Chung-Han Lee, MD, of Memorial Sloan Kettering Cancer Center; Yoshihiko Tomita, MD, of Niigata University; Martin H. Voss, MD, of Memorial Sloan Kettering Cancer Center; Elizabeth R. Plimack, MD, of Fox Chase Cancer Center; Toni K. Choueiri, MD, of Dana-Farber; Brian I. Rini, MD, of Vanderbilt Ingram Cancer Center; Hans J. Hammers, MD, of UT Southwestern; Bernard Escudier, MD, and Laurence Albiges, MD, both of Gustave Roussy; Stephen Huo, PhD, Viviana Del Tejo, PharmD, and Brian Stwalley, PharmD, all of Bristol Myers Squibb; and Michael B. Atkins, MD, of Georgetown-Lombardi Comprehensive Cancer Center.

This study was funded by Bristol Myers Squibb (BMS), Ono Pharmaceutical Company Ltd., National Cancer Institute Cancer Center Support Grants and a Dana-Farber/Harvard Cancer Center National Institutes of Health SPORE Grant for kidney cancer.

Regan reports research grants from Novartis, Pfizer, Ipsen TerSera, Merck, Ferring, Pierre Fabre, Roche, AstraZeneca, Bayer, and BMS; and consulting fees from Ipsen/Debiopharm, BMS, and Tolmar Pharmaceuticals.

This article was originally published on November 10, 2021, by Dana-Farber Cancer Institute. It is republished with permission.

© 2026 Smart + Strong All Rights Reserved.
http://beta.docker.cancerhealth.com/article/assessing-immunotherapy-benefit-specific-kidney-cancer-patients