Editor's Note

Clinical Decision Making in the Real World—The Perfect as the Enemy of the Good

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As clinicians, we strive to integrate the strongest evidence to support optimal management, but every day we are forced to make clinical decisions without comparative data providing a clear path. For patients with advanced non–small cell lung cancer (NSCLC) who receive an immune checkpoint inhibitor (ICI) as first-line therapy, whether as monotherapy or combined with chemotherapy, most clinical trials have limited the duration of immunotherapy to 2 years. But is that optimal? Five-year follow-up has found that 46.4% of patients with high tumor programmed cell death ligand 1 (PD-L1) expression who received treatment with pembrolizumab monotherapy during the KEYNOTE-024 trial before discontinuing at 2 years remained alive without further treatment or disease progression[1]; in the KEYNOTE-407 trial of patients with advanced squamous NSCLC (with no restriction by PD-L1 expression) that administered chemotherapy/pembrolizumab for 4 cycles followed by maintenance pembrolizumab alone for up to 2 years, 43.6% of those who completed 2 years of treatment remained alive without progression or subsequent therapy at the last follow-up.[2] We can only speculate about whether the proportion of patients alive without progression would be substantially higher if treatment with immunotherapy continued longer.

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We can now add data from the retrospective cohort study by Sun and colleagues[3] that looks at overall survival (OS) of patients treated with first-line immunotherapy in a clinical database after receiving a diagnosis of advanced NSCLC. Starting with 14 406 patients who initiated treatment with first-line immunotherapy, the investigators focused on 706 who completed 2 years of therapy. The first key finding was that more than 4 of 5 patients who reached this landmark continued to receive immunotherapy rather than discontinuing it, reflecting a strong bias toward potential overtreatment vs possible undertreatment. However, 2-year OS from the 760-day landmark was nearly identical for those who discontinued vs continued beyond that time (79% vs 81%, respectively), with no significant difference in OS on univariate or multivariable Cox regression.

There are clear limitations in retrospective clinical data. We may want to wait for prospective randomized clinical trial data, but this will be a difficult study to complete, and results will take many years to become available. In the meantime, the perfect should not be the enemy of the good: these data may provide reassurance to us and patients that discontinuing treatment at 2 years can confer the same OS as extended treatment with lower risk of toxic effects, less time in treatment for patients, and considerably lower costs for our health care system.

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