Neoadjuvant nivolumab shows long-term benefit in patients with non–small cell lung cancer

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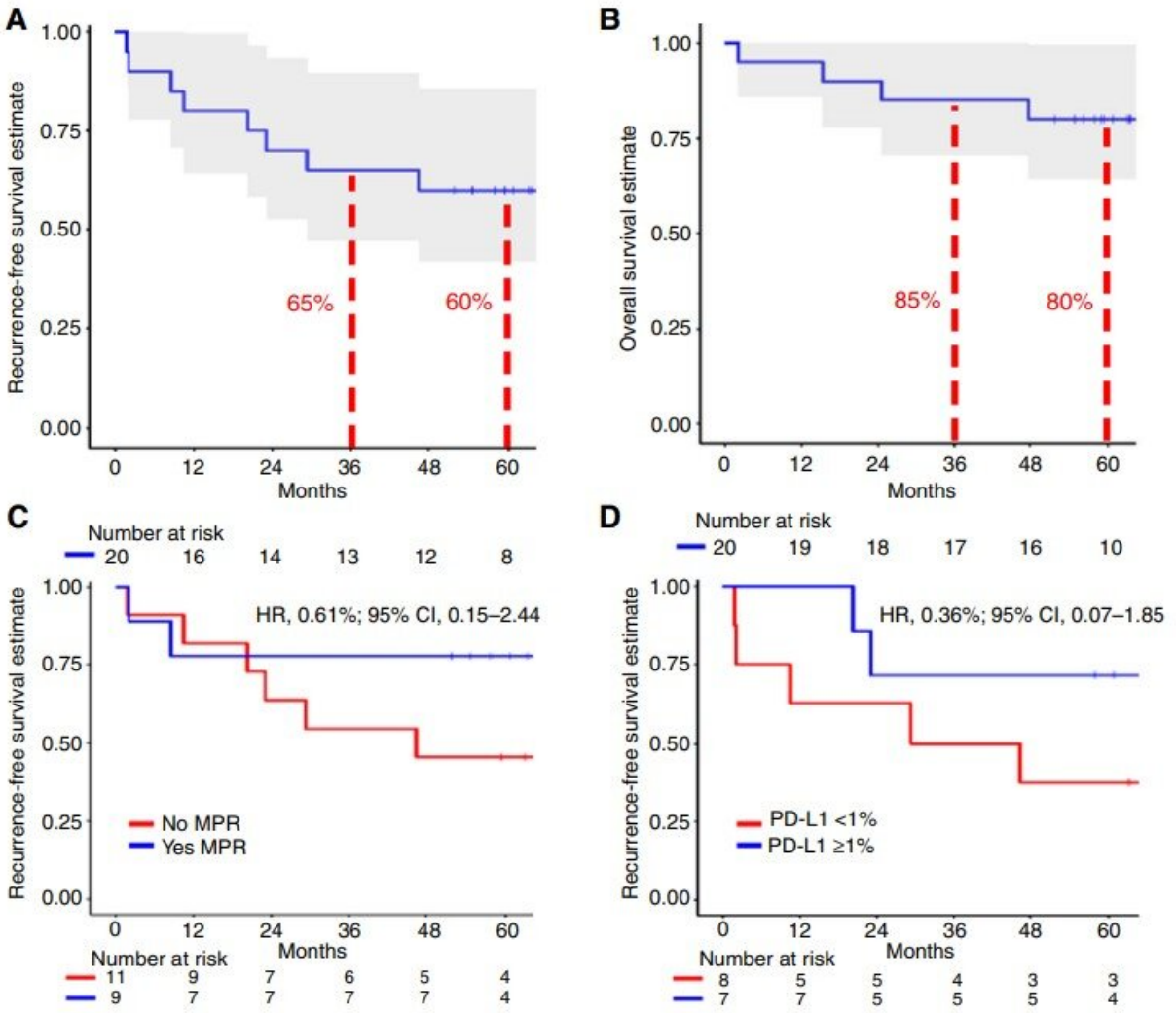

A–D, Kaplan–Meier curves depicting the recurrence-free survival (A) and

overall survival (B) for patients who underwent definitive resection after receiving neoadjuvant nivolumab. C, Depicts the recurrence-free survival for patients with or without major pathological response after neoadjuvant nivolumab. D, Shows the recurrence-free survival stratified by pre-treatment tumor PD-L1 expression. The dashed lines represent the 95% confidence intervals for each KM-curve. Abbreviations: Major pathological response, MPR; Programmed death-ligand 1, PD-L1; Hazard ratio, HR; Confidence Interval, CI. Credit: *Clinical Cancer Research* (2023). DOI: 10.1158/1078-0432.CCR-22-2994

Patients with resectable non–small cell lung cancer (NSCLC) who were treated with neoadjuvant nivolumab had improved five-year recurrence-free and overall survival rates compared with historical outcomes, according to results published in *Clinical Cancer Research*.

NSCLC is the most common type of lung cancer and is a leading cause of cancer-related death worldwide. Despite strides in treating metastatic NSCLC, new treatments for earlier-stage disease have only recently emerged, according to the study's senior author, Patrick Forde, MBBCh, an associate professor of oncology and director of the Thoracic Oncology Clinical Research Program at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins.

Samuel Rosner, MD, co-first author of the study, added that there is great interest in optimizing neoadjuvant strategies for earlier-stage NSCLCs that are eligible for surgical resection. Rosner is a medical oncology fellow at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins and a member of Forde's research group.

Forde, Rosner, and colleagues previously reported safety and efficacy results from a phase II clinical trial in which patients with stage I-III resectable NSCLC were treated with two doses of neoadjuvant

nivolumab. Major pathological responses were observed in 45% of patients, independent of tumor PD-L1 expression, and 73% of patients whose tumors were surgically resected were recurrence-free 18 months following surgery.

The latest publication reports the final analyses from this trial, including five-year recurrence-free and overall survival rates for the 20 patients who underwent surgical resection.

"To our knowledge, this is the longest follow-up to date for a PD-1/PD-L1 inhibitor in the neoadjuvant setting for any solid tumor," said Forde.

Among the 20 patients who underwent surgical resection, 12 patients (60%) remained recurrence-free five years after surgery, and 16 patients (80%) were alive, exceeding the 36% to 68% five-year survival rate historically observed for patients with stage I-III NSCLC, Rosner noted. Forde added that the observed patient outcomes after neoadjuvant nivolumab were better than those historically observed among patients treated with neoadjuvant chemotherapy.

The authors also identified major pathologic response after neoadjuvant nivolumab as a potential predictive biomarker of recurrence-free and overall survival. Of the nine patients who had a major pathological response after neoadjuvant nivolumab, eight were alive and cancer-free five years after treatment. One patient experienced a recurrence within the first 10 months after treatment but has since been disease-free after definitive chemoradiation. The one death in this subgroup was unrelated to cancer.

In contrast, six of the 11 patients who did not have a major pathological response experienced disease recurrence, and three of these patients died due to their cancer. These results indicate that a major pathological response following neoadjuvant nivolumab may be associated with a

lower risk of disease recurrence and death, although the authors caution that these results are preliminary and require further validation in larger studies.

Neoadjuvant nivolumab did not lead to surgical delays, and there was only one late-onset immune-related adverse event, which occurred 16 months after nivolumab treatment and was successfully managed, the authors noted.

"The results from the five-year follow-up analysis indicate that neoadjuvant nivolumab was safe in long-term follow-up and led to encouraging survival in this patient cohort," said Forde. "The long-term safety and efficacy data from this study provide further support for the use of nivolumab in the neoadjuvant setting."

Neoadjuvant nivolumab in combination with chemotherapy was approved by the U.S. Food and Drug Administration in March 2022 for the treatment of lung cancer. "Further studies will help us determine whether select patients may benefit from immunotherapy alone," Forde noted.

"An interesting finding from the analysis was the difference in outcomes between patients with and without a major pathological response," said Rosner. "Although the sample size was small, the results illustrate the potential power of pathological response as a predictive biomarker."

Limitations of the study include the small cohort size and the single-arm design.

More information: Samuel Rosner et al, Five-Year Clinical Outcomes after Neoadjuvant Nivolumab in Resectable Non–Small Cell Lung Cancer, *Clinical Cancer Research* (2023). DOI: 10.1158/1078-0432.CCR-22-2994

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