Commentary: To whom much is given much will be required

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The clinical interest of immune checkpoint inhibitor (ICI) is shifting toward surgically resectable non–small cell lung cancer (NSCLC) after the favorable outcomes associated with its use among the nonresectable advanced or metastatic patients with NSCLC. The year 2021 was an exciting year for us to see the promising results of clinical trials for neoadjuvant immunotherapy for resectable NSCLC, including the Neoadjuvant Nivolumab or Nivolumab plus Ipilimumab in Operable Non–Small Cell Lung Cancer (NEOSTAR) trial, Lung Cancer Mutation Consortium-3 trial, and Checkmate-816 trial.

The NEOSTAR trial was a Phase II clinical trial that enrolled 44 patients with stage IB through III NSCLC. Eligible patients were assigned to either nivolumab monotherapy or nivolumab plus ipilimumab dual therapy. The primary outcome of NEOSTAR was the major pathological response (MPR). Sepesi and colleagues report the detailed outcomes of the NEOSTAR trial from a surgical perspective. Of the total 44 patients, 37 patients (84%) (21 of 23 [91%] after monotherapy and 16 of 21 [76%] after dual therapy) underwent surgical resection. The primary end point of MPR was achieved with nivolumab monotherapy and with nivolumab plus ipilimumab in 22% and 38% of these arms, respectively. The authors subjectively graded the difficulty of surgical resection, considering grade 2 as average complexity. In 15 cases (40%), the surgical complexity was considered more challenging, necessitating more sharp dissection for the obliterated or fibrotic anatomic planes. This resulted in significantly longer operative times and higher estimated blood loss. Of the 12 cases that were planned to be performed minimally invasively using either the thoracoscopic or robotic platform, 2 (17%) were electively converted to open. And there were 9 patients (24%) who had pulmonary complications, including 1 mortality from bronchopulmonary fistula. Cumulatively, the evaluation of the surgical outcomes associated with the NEOSTAR trial underscore the need for thoracic surgeons to perform at the pinnacle of their abilities when operating in the context of neoadjuvant ICI.

Overall, the results of the NEOSTAR trial indicate that adding ipilimumab to nivolumab gives great hope for a better future associated with locally advanced NSCLC. From a surgical standpoint, MPR enduring the test of time as a predictive marker for improved overall or event-free survival may become an issue of significance, especially in light of the increased operative demands placed on thoracic surgeons. Until then, the integration of ICIs into new neoadjuvant treatment paradigms for NSCLC is emerging as among the most enlightening eras for thoracic surgeons. The description of the surgical outcomes associated with this new paradigm strongly suggests that there will be a need for an advanced and superior surgical skillset that are required to achieve technical success in the operating room. In turn, this greater surgical skill has the potential to lead to longer-term benefits associated with neoadjuvant treatment for NSCLC.
ICI and anatomic lung resections. In many ways, this prospect is a gift to the skilled thoracic surgeons who will be given the opportunity to provide a benefit to those patients who face the daunting task of battling locally advanced NSCLCs and who once had limited options. Furthermore, the ability to meaningfully affect change through performing at our best should resonate with us because it is one of the underpinnings for our passion for thoracic oncology surgery. As is the case for all high-achievers, preparation will be the key. Armed with what Sepesi and colleagues have presented, thoracic surgeons undoubtedly will be better equipped to meet the technical challenges that are required to give patients the best possible outcomes.

References