Editorial

Lung resection and immunotherapy: two allied for a new hope in lung cancer cure

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In the present article, Dr. Bott and associates (1) seek to address the absorbing question of the safety and utility of pulmonary resection in the setting of patients with residual disease following immune checkpoint inhibitors. For this purpose, data from 19 patients who underwent 22 resections for suspected residual disease, with therapeutic intent, following immunotherapy over a 5-year period (2012–2016) were queried and retrospectively assessed. The authors indicated the following points: (I) the 2 most common diagnoses were lung cancer (47%) and metastatic melanoma (37%); (II) nivolumab, pembrolizumab, and ipilimumab were the most frequently used agents (respectively 32%, 32%, and 16%); (III) a mean of 21 doses (median, 16; range, 1–70 doses) was given to patients; (IV) mean duration from final treatment to surgery was 75 days (range, 7–183 days). The results showed that lobectomies or greater anatomic resection were performed in 11 cases (50%). Importantly, 4 lobectomies were attempted minimally invasively. Of the 11 wedge resections, 10 were minimally invasive wedge resection. Of the 22 resected patients, 68% had viable tumor remaining on final pathologic assessment. Mean operative time for lobectomy was 227 minutes (range, 150–394 minutes). Complications occurred in 32% of cases. Most complications were minor in severity (grade 1/2). Two-year overall survival (OS) and disease-free survival (DFS) were 77% (95% CI, 58–100%) and 42% (95% CI, 25–71%). Finally, the authors concluded the following: (I) lung resection for suspected residual disease following immunotherapy appears to be feasible, with 95% of R0 resection, in patients with previously metastatic or unresectable cancer; (II) although surgery can be demanding, significant morbidity happens rarely; and (III) outcomes are promising with acceptable survivals during the short-term follow-up.

One might ask why the thoracic surgical community should be concerned with the findings of this study? Not only because this invigorating paper suggest another treatment pathway—and hope—for this specific category of patients; rather because we will probably have to learn how to manage with resections following immune checkpoint inhibitors in a quite close future. It can already be the case, as reported in this publication, in metastatic settings, in order to resect residual primary or local foci. It will be even more frequent when the numerous clinical trials [evaluating in a neo adjuvant setting almost all the anti-programmed cell death 1 (PD-1), anti-programmed cell death ligand 1 (PD-L1) or anti cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) approved in metastatic lung cancer] will be finished. The preliminary results of the NADIM trial, assessing the impact of 3 cycles of nivolumab + platinum-based chemotherapy given 3 to 4 weeks before surgery (and then followed by nivolumab alone in adjuvant setting

for one year) in stage III lung cancer patients, have been recently presented in the International Association for the Study of Lung Cancer (IASLC) meeting in Toronto (2). The primary end point was progression free survival but the presentation focused on the postsurgical complications, concerning 7/30 patients. The most frequent complication was infection (respiratory infection in 3 patients and post-surgery pneumonia in one). There was no post-operative mortality. The most interesting result could be the rate of pathologic response. Indeed, the author noticed a major response (<10% of viable tumor cells) in 80% of resected cases (with 75% of complete response). These results are consistent with the results published by Forde *et al.* (3) showing a major response in 45% of the patients, treated by only 2 cycles of nivolumab in neoadjuvant setting. It's communally admitted that a major response can be considered as a surrogate marker for survival (4). Of course, we'll have to wait the data regarding the progression free survival and the overall survival, but we can clearly anticipate that immune checkpoint inhibitors—alone or associated with chemotherapy—will shortly become a standard in the neo-adjuvant setting.

Moreover, the article of Fournel and colleagues (5) provides a wealth of information on adjuvant surgery following treatment with tyrosine kinase inhibitors (TKI) in patients with advanced lung adenocarcinoma. In their cohort of 19 highly selected patients, the authors nicely showed a large spectrum of histopathological changes in their specimens and promising preliminary survival results (the 3- and 5-year OS and DFS rates were 79.5%/39.8% and 44.4%/29.6%, respectively). The authors concluded that, pending further research, adjuvant surgery following treatment with TKI may be considered as a relatively reliable and safe therapeutic choice, in case of lobectomy. However, in case an extensive resection—pneumonectomy—is to be planned, the authors were more cautious and did not recommend adjuvant surgery.

Be that as it may, the current article contributes to successfully "opened one door leading to ten more" in the burgeoning field of immunotherapy. Future works on immunotherapy and surgery (for advanced or unresectable disease) should examine not only resection rate but also survival as primary objectives. It may be the clue to altering some prominent oncologic dogmas, and thus the established decision of therapeutic indications. For now, Dr Bott and colleagues (1) are to be congratulated on their innovative contribution in this area. From the standpoint of medical care, their results will certainly affect future patient management.

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Footnote

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