Commentary: Neoadjuvant Immunotherapy followed by Lung Cancer Resection: Is the Future Already Here?

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Central Message: Immunotherapy will be an important part of multi-modal lung cancer treatment paradigms. Studies designed to understand this are needed.

Central Picture Legend: Rishindra M. Reddy, MD, MBA

Kumar et al perform a retrospective review of an administrative database evaluating the use of immunotherapy for locally advanced lung cancer (cT1-3N2), comparing the use of definitive concurrent chemoradiation followed by immunotherapy (cCRT + IO) to the used of induction chemoinmunotherapy followed by surgery (CT/IO+Surgery) (4). They found improved 3-year survival in the surgery group comparing the groups overall, and after propensity matching. The authors are appropriately measured in their conclusions with their emphasis that these results should be hypothesis generating. Immunotherapy will change who we operate on in the future. There are limited takeaways though from this study due to the constraints of the study design, including the use of an administrative database, the fact that most of the surgery patients were likely on a clinical trial, and that Stage IIIB patients were included.

One can not use administrative databases to compare different clinical choices, as they lack the ability to understand the decisions on why a treatment choice was made. The National Cancer Database (NCDB) only tracks overall survival, not disease-free survival, and lacks data on performance status, which clearly impacts the choice for surgery as being a part of the treatment paradigm (1).
Aside from the use of an administrative database for this study, it is clear from the timing of the dataset (2013-2020) that most, if not all the surgical patients were on clinical trials. This leads to a biased group of patients in the surgical arm, that tend to be younger with fewer co-morbidities than those who were not on a clinical trial (2). A key problem with most clinical trials is that they don’t include older and more frail patients. Kumar et al found that the non-surgery cohort was approximately 4 years older than the surgery cohort in their study, prior to matching. Even after matching for age and other variables, there was no way to match for performance status, which alone could explain the 3-year survival difference between the cohorts. There is no way to address this bias with the current study design and the authors acknowledge this is in their discussion.

My last concern was the inclusion of Stage IIIB patients (T3N2) in this study, and there appears to have been a trend towards more T3 tumors in the non-surgery group compared to the surgery group (p=0.08). Although this wasn’t statistically significant, could this higher rate of IIIB patients in the non-surgery arm contribute to the worse outcomes? Surgery is not routine for most patients with Stage III lung cancer, let alone Stage IIIB (3). Given this, the inclusion of these patients in the comparison arm of the non-surgical group will certainly lead to lower survivals. Overall, Kumar et al share interesting data that should spark interest in a broader look at the use of immunotherapy in lung cancer. The ability to interpret the comparison arms though are limited.
References


