Discussion to: Salvage Lung Resection after Immunotherapy is Feasible and Safe

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Discussion to: Salvage Lung Resection after Immunotherapy is Feasible and Safe

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Disclosures: None

Dr. Anthony W. Kim (Los Angeles, CA):

Thank you. I'd like to thank the AATS for the opportunity to discuss this paper, and I'd like to congratulate Dr. Nemeth and his esteemed colleagues for collaborating on both a timely and important topic. I'd also like to thank them for forwarding the manuscript in advance of this meeting. In the NCDB study, they demonstrate that what they deem to be salvage resections are not associated with the worst perioperative metrics, such as readmissions and 30-day and 90-day mortality rates when compared to salvage resections following chemoradiation therapy. I think the additional pearls in the study come in the form of lobectomies being the predominant operation, indicating the absence of routine need for extended resections such as pneumonectomy. Of further interest is that when pneumonectomies are required, the mortality burden is sometimes observed with more traditional therapies is not observed. Cumulatively, I think this information is important because it informs many thoracic surgeons that the salvage resection paradigm is worth pursuing. With that said, I believe the authors should offer some additional commentary to provide some sage advice in this domain to better equip the practicing thoracic surgeon to work in this paradigm wisely.

So, my first question is, according to the NCDB data dictionary-- and as you note in the manuscript, an update to the PUF to recategorize certain chemotherapeutic medications to pneumotherapy was made in 2013. That said, the six drugs they included were - forgive the mispronunciation - alemtuzumab, bevacizumab, rituximab, trastuzumab, pertuzumab, and cetuximab. None of
these medications have been the ones included in now the landmark clinical trials published showing benefits and disease-free survival. I'm sure since 2013, the NCDB incorporated many of the more recent immunotherapies included in these trials. That said, though, the larger phase 2 and phase 3 trials, such as the LCMC3, NADIM, NEOSTAR, CheckMate 816, IMPower030, and AEGERAN trials evaluating the different combinations of therapy, all began their enrollment in 2016 or after. So, therefore, do you think the results would change had you exclusively evaluated these more relevant agents? And along these lines, do you think there would be any benefit to starting the analysis after 2016?

Dr. Attila Nemeth (Tübingen, Germany):

Thank you very much for the comments. I think this is a big limitation of the study, because we don't know exactly which drugs were used. We don't know the time points. Was the therapy started, for example, with chemoradiation? Was it started with immunotherapy or drugs that are not considered direct immunotherapy? It would be interesting to have, firstly, a larger number of patients to have the possibility to analyze it, and it's definitely something as a future perspective.

Dr. Kim:

Okay. Great. I appreciate your comments in the manuscript regarding how the five-month mark was determined as the cutoff for salvage therapy, and while the five-month window is reasonably late enough to constitute an appropriate time frame, salvage often denotes a longer interval. And so, your better survival, albeit not statistically significant, was at greater than nine months. And this speaks to perhaps a different disease process than those that require a salvage resection, say, at five months. So, with this in mind, and understanding that the NCDB cannot provide insight as to the reason for pursuing the salvage resections, can you posit some of your practical theories as to what the differences and the indications and disease processes possibly could be? And I can't put my finger on it, but I wonder if some of it has to do with the fact that you included some stage I patients as well? I may be wrong.

Dr. Nemeth:

Yeah. That's another limitation. First, we considered five months as a time point to exclude the patients that were undergoing neoadjuvant therapy. That was because most of them are around 90 days, so three, four months, or five months was considered to be reasonable to take into the study as a time point. Secondly, I didn't include these results about more than nine months having a slightly better survival. But probably it's due to-- longer survivals or time periods where the patient did not get any metastasis are probably a better factor for survival. And regarding the stages, I showed a slide at the beginning where we had a
couple of patients that were in stages I and II. We cannot opt out if these were patients in trial. We don't know if these were patients that were initially not treated or not operative patients. We don't have any data about lung function, if that's mainly a reason.

Dr. Kim:

Okay. Last question. Promise the torture will stop. You've included wide resections in your studies. How can you assure us that this type of resection truly represented a curative intent procedure? I raise this issue because of all the recent attention garnered by sublobar resections, while well deserved, may not be translatable to the salvage setting. Furthermore, I shudder to think that the art of anatomic resection may be falling by the wayside. And in circumstances such as clinical stage of diseases that warrant immunotherapy, there's a need to be the best oncologic surgeon. Some clinical trials had excluded wide resections. Therefore, could you opine as to whether you truly believe that wide resections truly are in the best interest of patients in this exact setting?

Dr. Nemeth:

Thank you. I think that, firstly, we need to look up the data of the pneumonectomies. We considered, or our initial thought was, that the rate of pneumonectomies would be much, much higher. And there are a couple of sublobar resections with wedge resections being the lowest ones. Again, I think these could be patients that didn't have enough lung function and were treated as salvage resections. We also know that-- we're getting more and more data that resecting lung tissue without cancer maybe does not have additional benefits. But I don't consider wedge resection as a perfect solution in these kinds of patients. Most of them are lobectomies or anatomical resections and have feasible results.

Dr. Kim:

Right. Thank you again, and congratulations on your important contribution.

Dr. Nemeth:

Thank you very much.

[applause]