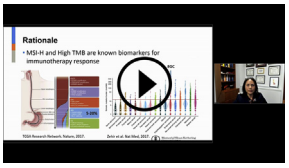
studies of larger groups of patients will be needed to confirm these results. Full reporting of the results of the clinical trials discussed here, in terms of pathologic response rates, survival, and genomic correlatives, will be forthcoming in future work, once target accruals are met.

Webcast

You can watch a Webcast of this AATS meeting presentation by going to: https://aats.blob.core.windows.net/media/20AM/Presentations/Safety%20and%20Feasibility%20of%20Esophagect.mp4.



Conflict of Interest Statement

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The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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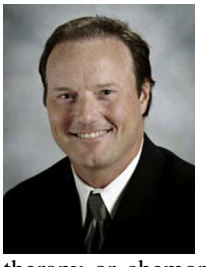
Key Words: esophagectomy, immunotherapy, chemoradiotherapy, esophageal cancer

Discussion

Presenter: Dr Smita Sihag



Dr Wayne L. Hofstetter *(Houston, Tex)*. Congratulations, Smita, on a really nice paper; very well presented. First of all, I'd like to congratulate the group for recognizing that we are not making headway in the treatment of locally advanced esophageal cancer by debating different types of chemotherapy or chemoradiation. The need to move the needle forward is apparent, and bringing therapeutic options like immunotherapy to the clinical setting is critical. So

congratulations on engaging in these protocols in the first place.

My first question for you is: Based on data not presented—based on just your eyes and your hands—were there any differences in operating on patients who have had immunotherapy compared with those who did not? Were these cases harder at all?

Dr Smita Sihag *(New York, NY)*. Thank you very much, Dr Hofstetter; great question. We have not studied this formally and perhaps we should, but in an informal polling amongst my colleagues that have done these cases, we have really not appreciated any greater difficulty associated with the dissection during these cases following immunotherapy.

Obviously, these cases are hard to begin with, following chemoradiotherapy, but I would say that we have not appreciated any major differences with the addition of immunotherapy. We do think that there is probably a difference in the quality of fibrosis that we see, but as such, no increased difficulty.

Dr Hofstetter. I think that's relatively interesting because with the lung, we've recognized that there's sometimes often a significant difference in difficulty. Do you think that as we start doing tumors that are maybe a little bit higher up, say in the midesophagus rather than an easier area like the esophagogastric junction where your protocols focused, that we may start running into more fibrosis around the airway specifically? And what about larger tumors—were you able to look at smaller versus larger tumors?

Dr Sihag. That's a terrific point. Obviously, the patients selected for these initial clinical trials are somewhat cherry-picked and so far we have not encountered very bulky tumors—T4A tumors in particular and so forth—that might be difficult to dissect off the airway or the pericardium. Therefore, as our experience evolves, we may actually notice more of a difference. But at this time, I would say that most surgeons in our group agree that there is no increased difficulty.

Dr Hofstetter. Smita, how did your team define response? Obviously, we can define it in terms of the tumor regression grade response just in the primary tumor. Did you also take a look at response within the lymph nodes? And, in the particular episode where you said there was 90% downstaging—did that result in actual pathologic downstaging of the tumor?

Dr Sihag. Yes, thank you for this question. So we did see nodal downstaging in 5 patients, and all of these patients had >90% treatment response in the primary tumor bed. I should mention that treatment response as defined in my slide refers to treatment response in the primary tumor bed only. So it does not account for nodal status or residual nodal disease. But 5 patients in this particular group actually did have evidence of treatment effect in the lymph nodes. The median number of lymph nodes that were harvested in our immunotherapy cohort in comparison to the control cohort were similar at 22, and overall downstaging was seen in 19 or 73% of patients in the immunotherapy cohort, as opposed to only 58% of patients in the control cohort.

Dr Hofstetter. That's great. You've really answered the question of whether we can do it; there's some nervousness about moving forward with surgery in a setting of chemoradiation and immunotherapy. I guess the next real question is: should we be doing this, and do these treatment responses just reflect heterogeneity in your patient population, or are these really related to the addition of immune therapy? So I'll be really looking forward to the outcomes of these studies.

Dr Sihag. Yes, I agree. Thank you very much.

Dr Hofstetter. That concludes my questions. Great job, Smita; thank you. And thank you for having me discuss.

Dr Christine L. Lau *(Baltimore, Md)*. Smita, where do you plan to take this from here on out? And if you had any patients that are further than eight weeks out that have had any problems with fibrosis, I'm assuming you continue the trial. Have there been any patients that have gone further out that have not been operated on within eight weeks?

Dr Sihag. Sure, that's a great question. Thank you, Dr Lau. At this point, we do have some longer-term outcomes on some of these patients and we'll actually be able to report 90-day outcomes in our manuscript. In terms of cases where we've had long delays to surgery, we actually have not had any significant delays at this point. The protocol dictates going to surgery within 6 to 8 weeks in our usual, standard fashion, after completing neoadjuvant therapy (including immunotherapy) and our goal has been to try to get patients done in that interval, on this protocol especially.

Dr Lau. Thank you.