Transcript Details
This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/neoadjuvant-or-adjuvant-immunotherapy-in-early-stage-nsclc-is-there-a-preferred-strategy/14580/

Released: 11/30/2022
Valid until: 11/30/2023
Time needed to complete: 2h 36m

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Neoadjuvant or Adjuvant Immunotherapy in Early-Stage NSCLC: Is There a Preferred Strategy?

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCME curriculum.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Forde:
So, we are here with you today to discuss considerations for neoadjuvant versus adjuvant therapy for non-small cell lung cancer. It is a hot topic at the moment in medical oncology, surgical oncology, and pathology. And first, I am going to go to Dr. Peters to ask her for some thoughts she has when thinking about neoadjuvant versus adjuvant.

Dr. Peters:
Yes, thanks a lot. I guess it is that the main concern we have, right? In term of trying to understand if there is a biological and clinical outcome benefit by delivering neoadjuvant versus adjuvant. We are traditionally more used in a standard manner to administer adjuvant treatments, adjuvant chemo. Now, it is CHEMO-IO. So, are we going to switch all these patients to neoadjuvant? So, I guess we have more and more data telling it is safe. And it might be in term of magnitude even more efficacious and active that we would have sought. But let us keep in mind also that in each of our countries we have a landscape of practicalities, right? Which might make the surgeon coming second being a different difficult concept to introduce, right? So, what I mean by that is I am more and more encouraged to go to neoadjuvant because of compliance and some biological statements that we could cover in another episodes. But the other thing is how you can really be implemented through tumor board or sometimes without a tumor board being existing.

Dr. Forde:
Yes, I think that is a great sequence into talking with Dr. Spicer, a thoracic surgeon from Canada on how he approaches neoadjuvant therapy as a surgeon, potential considerations around toxicity, delays to surgery. Are there real considerations and immune-related events? And how you deal with that neoadjuvant period. Jon?

Dr. Spicer:
Yes, thanks, Dr. Ford. So, I was already sort of bought into the concept of neoadjuvant chemotherapy for most patients who would have met indications for adjuvant based on their clinical staging. So, this is, you know, size more than four centimeters, stage of classic AJCC-7 Stage IB to IIIA. So, we are already in the mode for quite some time of giving preoperative standard chemotherapy even to Stage IIA or IB patients. Although I realize that that is not a common approach internationally. Part of the reason we had adopted that view is that we had a very good transition to surgery. So, the vast, vast majority of patients in our in our center were making it to the operating room. And the from a toxicity standpoint there is data to support the notion that the treatment is better tolerated when given preoperatively than postoperatively. And we know that only about 60% of patients in the best-case scenario will actually get adjuvant chemo. So, with the, again, the idea of giving a full course of treatment to people that we know will benefit from systemic therapy that serve our bias to giving preoperative. Now, I think it is important to understand that with that lens, neoadjuvant therapy does have perhaps a tendency to overtreat some of these patients who might be cured by surgery alone. And maybe poses some challenges that Dr. Cottrell could talk to us about with regards to getting the right biomarkers at the right times that we do not incur those delays in terms

of patient treatment.

Dr. Forde:
Yes, I think that is a key point in terms of getting to treatment. We had data very recently here in the U.S. from the ALCHEMIST trial, which was a large phase 3 trial enrolled fit patients who should have been eligible for adjuvant chemo. And even in that trial setting, only about 57% of them received any adjuvant platinum-based chemo. So again, those are hard discussions probably the longest discussions we have in clinic. So, in terms of adjuvant therapy and discussing with patients that you are treating a lot of people for small benefit. Hopefully, more benefit with CHEMO-IO and IO, but still tough discussions. Dr. Cottrell, could you comment on assessing pathological response after neoadjuvant therapy and some of the data we saw in CHECKMATE-816 and how that might be operationalized in your pathology lab, for example?

Dr. Cottrell
Yes, I think we saw some really exciting data in CHECKMATE-816. And specifically, we assessed tumor regression or treatment effect in the tumors. And we found that that correlates with event-free survival. And hopefully as the overall survival will data matures, we will have great evidence that this approach is going to be high value for patients. And I think there are two key sort of added value points for pathologic response that make neoadjuvant therapy advantageous over adjuvant. One is that first of all, we get an early readout of whether or not this patient actually responds to this regimen. And with adjuvant therapy, you have to sort of wait to see if the patient recurs or metastasizes. And then you can actually use that information to guide your adjuvant therapy approach. So, if a patient is not responding to your neoadjuvant immunotherapy plus chemotherapy, it may be worth considering an alternative approach in the adjuvant setting. So, I think there is a lot of exciting and important work to be done in this space.

Dr. Forde:
Yes, I agree. I think that pathologic readout is very useful. So, in CHECKMATE-816, we saw that at about 2 years if you had a pathological complete response, which was no residual tumor at the time of resection. Those patients had more than 90% of entry survival at 2 years. Versus if you did not have a pathologic complete response, it was down around 50%. And Dr. Peters, you could envision scenarios potentially on how those patients might be addressed differently in the adjuvant setting, perhaps.

Dr. Peters:
Yes. Well, there is still a question mark for me in these trials because we observe what happens to subgroups of patients according to the quality of pathological response. It does not mean that you know what to do with them, right? We will see a series of trial coming very soon with what we call sandwich operative strategy where they receive neoadjuvant CHEMO-IO and an additional almost one year of immunotherapy. So, it does not mean that you have not, if you have not reached a pathological complete response or a major pathological response that you do not extract benefit from a longer duration of IO. That is another scientific question where you should randomize this patient with a certain degree of response to yes or no continuation. So, we will observe, we will try to compare but still there might be a reason to continue IO even if you have not met a pathological complete response or an NPR. Meaning that, of course, stratum gives you an idea of the prognosis and the chance of being relapse free, but it does not mean that the intervention you do has no value in a poor prognostic setting, right? So, I think there are many questions that we will have to answer for each of these categories of patients, which still will not be, we should not shortcut, right? We should not make decision too fast because it might be then a patient with 50% pathological response only 50% might have an additional value of getting nine cycles of pembrolizumab, nivolumab durvalumab or whatever. And this will not be answered by clinical trials even if we would be disappointed. It does not mean that there is no value. So, we have to be careful about it. We have to observe many trials and try later on maybe in the academic setting to ask the right questions about how long, how much, and to whom. But this will not be answered in an evidence-based manner by these trials.

Dr. Forde:
Yes. I think those are important points. We are seeing kind of a very rapidly evolving field where for 10 years we had no perioperative trials. And now, we have three large… or four, I guess, three. I am trying to remember. Four large trials reported in the space of 2 years. If you counted DORA. Jon, just to get back a little bit to your kind of how you address these patients in the preoperative setting are you concerned about surgery being delayed? Do you do anything in particular in terms of prehabilitation, which is the idea of improving patient's functional status for surgery? How do you deal with a patient who is actually receiving neoadjuvant CHEMO-IO?

Dr. Spicer:
Yes, so these are great questions. I think it is important to remember that CHECKMATE 816 was patients who were operable. So, we if we were going to approach patients for this debate, they have to be operable at a baseline and that is what is going to translate to a good rate of progress to surgery after neoadjuvant and minimize delays. We have found that pairing the neoadjuvant therapy with a comprehensive prehabilitation program to mitigate medical comorbidities, to make sure nutrition, and exercise programs are paired with these treatments is quite helpful to make sure that they get to the operating room in the best condition possible and that this seems to

translate to good outcomes postoperatively. So that, that is very important. You know, the simple thing for me is that if they have clinically evident disease that merits systemic therapy, given the limitations in terms of our understanding around biomarkers we tend to advocate for CHEMO-IO. Providers know EGFR mutation. But that all the advances that have been made in the adjuvant setting are extremely valuable to all the incidentally identified N I and II patients who go for upfront resection or who have conditions that prevent systemic therapy like a post-obstructive pneumonia. Maybe, those patients are better off going directly to the operating room or massive hemoptysis or chest wall invasion with significant pain that might not respond so well to preoperative treatment. So that is sort of how we kind of contextualize those scenarios.

Dr. Forde:
Perfect. Well, I think that it has been a good discussion and we have several other episodes in this series where we have addressed some of the other questions, which arise around neoadjuvant and adjuvant therapy. And thank you all for joining us today.

Announcer:
You have been listening to CME on ReachMD. This activity is jointly provided by Global Learning Collaborative (GLC) and TotalCME, Inc. and is part of our MinuteCME curriculum.

To receive your free CME credit, or to download this activity, go to ReachMD.com/CME. Thank you for listening.