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<https://reachmd.com/programs/cme/tips-and-tricks-for-surgeons-managing-post-neoadjuvant-care/14579/>

Released: 11/30/2022

Valid until: 11/30/2023

Time needed to complete: 2h 36m

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### Tips and Tricks for Surgeons: Managing Post-Neoadjuvant Care

#### Announcer:

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

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#### Dr. Spicer:

My name is Jonathan Spicer, and I am a thoracic surgeon practicing up in Montreal, at McGill University here in Canada. This section will be on some of my Tips and Tricks for Surgeons: Managing Post-Neoadjuvant Care. So, I think the first and most important point for any surgeon looking to employ neoadjuvant chemo immunotherapy for a potentially resectable patient, is to choose the right patient to offer this to. I think in general, surgeons are accustomed to selecting their patients for surgery, because it is via the selection process that we identify patients best suited to benefit from the curative potential of an operation to resect lung cancer.

With that in mind, I think it is critical to realize that both CM816 and NADIM2, and all other periadjuvant phase 3 trials, for which pair pending results were designed to recruit patients who had operable disease at baseline. The goal of these studies was not to select patients with potentially resectable, or borderline resectable, or frankly unresectable disease, to treat them in the hopes that they might be downstage and become operable. So, what I think all surgeons should ask themselves when they see a patient in the clinic, and they are considering this approach, is could I get an R0 resection if I took this patient to the operating room today? And if the answer is no, then you are by definition, dealing with a borderline resectable disease. And while I do not have any objections to using preoperative chemo immunotherapy, with a goal of potentially resecting these patients, you cannot expect the same kinds of results as those that have been published to date, when you offer that kind of treatment plan to these borderline resectable patients.

The other issue is making a clear difference between what is resectable or operable anatomy, and what is adequate physiology to tolerate the operation required to have the right oncologic outcome. And this means the patient has to have adequate respiratory reserve, leaving sufficient capacity for good quality of life, based on the operation need, a baseline to achieve cure. I think it is critical to exclude patients who have EGFR or ALK alterations because they are unlikely to benefit from this treatment approach. In fact, could have their treatment course compromised as a result of potentially treating them with immunotherapy when they may be better addressed with other forms of treatment.

So, I think there is a lot we can do, in terms of restaging patients. There is not a whole lot of data to guide us about what to do, but my approach has really been to just do what is necessary and sufficient, keeping in mind that a lot of the tests that we can do, may generate information that is not particularly helpful, but will create a lot of questions that sort of need to be addressed. So, in summary, I think at a minimum, a CT chest with IV contrast is very helpful for surgical planning, and it will help rule out gross disease progression. And in my mind, this is a necessary element, and probably sufficient in most cases, with regards to restaging.

I think invasive media style restaging as a routine practice rarely changes the surgical plan and does not really need to be done in such a manner. I think it could be applied in the specific scenarios, where there is a serious concern about potentially unresectable, or contra lateral disease that needs to be ruled out. I have not been using PET imaging as a routine post-treatment because at least 10 to 20% of patients will have this phenomenon of nodal immune flare. And this can be quite problematic requiring us to do an invasive staging when

vast majority of the time, it will just be a benign inflammation, that is induced by the immune checkpoint inhibitors. There is data now on the effect of neoadjuvant chemo immunotherapy on PFTs, and there is really no clinically significant impact on lung function for this reason. I do not advocate repeating PFTs after pre-operative chemo immunotherapy.

I do think that pre-habilitation is extremely beneficial to our patients. We are fortunate at our hospital to have a team that does a full holistic evaluation of the patient, taking into consideration nutrition, exercise status, and psychological status, and will design a sort of a tailored plan for the patient to address and optimize medical comorbidities that are required further attention. Because a lot of folks may not be accustomed to doing preoperative therapy, I think having some sort of logistical workflow is helpful. So, the number one point is to really have clear lines of communication between the surgical team and those delivering systemic therapy. Things can occur on systemic therapy, that might change the plan. Perhaps patient develops a complication, needs to be on steroids, what should be the right timing of surgery? Perhaps they need to go surgery earlier than expected, because there is an intolerance to chemo or a reaction to immunotherapy that precludes further treatment. And so, it is really essential that there be a free flow of sharing of information, so that patients can be adequately navigated through this pathway. Second point is to involve pathology early. I think it is really important to have adequate material at diagnosis and staging to do biomarker testing. And if it is not something that is done reflexively in your center, if you think this patient is operable, please make every effort to get testing done as soon as possible, so there are no delays in care that result from this. I think the minimal discussion is one that needs to occur between a thoracic surgeon and medical oncologist. But ideally this is supported through a tumor board consensus, where radiation oncology is present, and all potential therapeutic options are explored for this patient. I think that in our environment, the surgeon consents and books the patient for surgery, at that initial visit because at least in our environment, all patients will go to surgery, and it is quite helpful to have them already on our surgical list to be able to better plan restaging investigations and timing of the OR. Once the patient has been seen by the surgeon, and deemed operable, and consented and booked, we try and get them to see the medical oncologist. If it is not in one of our multi T clinics, where they are seen together, the medical oncologist is to see within a short span of time and plans the first cycle of treatment.

Once the first cycle is dosed and planned, then it is very important for the systemic therapy team to communicate that back to the surgical team, so that we kind of have some expectations of when that third dose will be. And based on that we start tentatively reserving OR time for the patient. So really, they are not, the patients are not on a wait list but on sort of plan treatment program. And I find that helps with mitigating anxiety about you know, being on a wait list for surgery. These patients are all sort of on a clear program that has set timelines. I think action plans need to be set up in the event of complications that might arise during systemic treatment. And this comes back to the issue of communication. I think that some time needs to be allotted to allow for communication with the patient, regarding the results of restaging scans. And keeping everything in those narrow timelines can be a little bit challenging. So, it is important to have your clerical and nursing support staff kind of know what the plan is so that they can fit the visits in appropriately. And teleconferencing is a great way to touch base with patients, share that information, without having them necessarily come back to the hospital, especially when dealing with patients, who are further field, geographically. I think it is important for the OR and perioperative team anesthesia to all know, that these patients have received preoperative immune checkpoint inhibitors and that this can come with some adverse events that are unusual post-surgery. You know, we have seen patients develop hypothyroidism, be depressed, have pneumonitis. We have seen patients with adrenal insufficiency postoperatively. And so, these can present in a subtle manner at first, but can really impact the perioperative outcome. And so having a team, a perioperative team, that is alerted to these possibilities, I think important. I think the pathology requests, once you complete the operation, the specimen is in the bucket on its way to the lab. It should definitely be clearly labeled with regards to all the relevant preoperative information, ethnicity, smoking status whatever biomarker data might already be available, and definitely the type of preoperative therapy that was received, so that the pathologist can render the most pertinent result possible.

So, what about the postoperative care and surveillance of these patients? As I mentioned before, you have to keep the possibility of a subclinical immune related adverse event in mind. We have seen patients with hypothyroidism, adrenal deficiency, pneumonitis, but any organ can be affected. And so, you should know in your own institution, who are your resources, should you have someone such complications, into working collaboration with your treating oncologist to support you and your patient, should one of these kinds of complications be observed in the perioperative period. Thank you very much. Have a great day.

**Announcer:**

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