Gary Shelton (Moderator): Next to join Beth on the stage is Ms. Beth Gilbert. Beth is a PA and Lead Advance Practice Provider for the Head and Neck and Thoracic Medical Oncology team at Abramson Cancer Center, so she's with you. They'll be discussing managing early stage and locally advanced non-small cell lung cancer.

Beth Gilbert: All right. We saw all of these faculty financial disclosures. We're going to talk about non-small cell lung cancer in the early stage and stage III. Our learning objectives: we're going to devise treatment plans for patients with locally advanced, non-small cell lung cancer. Here's our outline, surgical approaches, we're going to touch on that with early stage, non-small cell work-up and staging, surgical approaches, non-surgical candidates. Stage III work up: treatment considerations, controversies, and with surgery and chemo/radiation.

Okay. You reading the question?

Beth Eaby-Sandy: I'll read the question, yeah.

Beth Gilbert: Sure.

Beth Eaby-Sandy: A 60 year old gentleman has just completed chemotherapy and radiation for his stage III non-small cell lung cancer, with weekly paclitaxel and carboplatin. He is here to discuss what would offer him the best survival advantage. Which would you counsel is the best optimal option based on the patients goals?

Is it immunotherapy for a year post-concurrent radiation, chemotherapy and radiation? Full dose consolidation therapy, followed by immunotherapy for one year? Stop with concurrent chemo radiation and go into a surveillance imaging scheduled every three month CAT scans? Full dose chemotherapy after the weekly chemo radiation, and then go into surveillance imaging every three months? Or unsure? (silence)

Yes?

Staff: Sorry, can I just make a point?

Beth Eaby-Sandy: Yes.

Staff: If you feel unsure about it, feel free to press the unsure button so that we can make sure that we note just how many of you-

Beth Eaby-Sandy: Yeah.

Staff: [crosstalk].

Beth Eaby-Sandy: Yeah, if you feel like you're unsure, go ahead and admit it because we don't know who you are when we are looking, so that's okay. Definitely, everybody please vote because that's how we get our metrics for learning.

Which drug or drugs are approved for locally advanced non-small cell lung cancer after completion of concurrent chemo/radiation when then cancer has not progressed? Is it pembrolizumab? Durvalumab? Nivolumab? Both A and B, or you're unsure? (silence)

Beth Gilbert: Okay.

Beth Eaby-Sandy: Okay.

Beth Gilbert: Very good. Here's the pie chart that we've already seen. The percentage of cases by stage, and we can see that 57% are distant metastatic, which is the unfortunate thing about lung cancer. We're going to talk about the localized, which is about 16%, and then regional, about 22%.

When we're saying, early stage, we mean stage I and stage II. With those two stages, generally, surgery is the best option. If not a surgical candidate, then they use radioablative or stereotactic body radiation, which I think is now called SABR.

Beth Eaby-Sandy: Yeah.

Beth Gilbert: Stereotactic ablative radiation.

Beth Eaby-Sandy: SABR.

Beth Gilbert: I love this chart.

Beth Eaby-Sandy: I don't.

Beth Gilbert: I love it. I have to refer to it all the time, but you have to look it all the time. I look at the N2, and how N2 dumps you into a stage III. It's kind of pivotal thing when you're doing staging for the patient.

When we're talking about staging...This is the one I love too, the nodal stations. Just having that handy is really a good visual to figure out what you're doing with the nodes. I had a question about this. We need to stage the mediastinum. Everybody gets a PET scan, and then you go by that PET or CT scan, then to figure out where you need to get your nodes. There's different ways to go about sampling the mediastinum with [bronch], EBUS. Depending on location, one modality may be better than the other.

One caveat, if it's negative on, when you get your EBUS, and you do your needle aspiration and the node is negative but the PET scan is still pretty hot, then you should do a mediastinoscopy prior to doing a resection. A lot of that, you really want to stage the patient before you decide their treatment plan and take them to surgery. That should be done prior to resection. I don't know if you've ever had any differences.

Beth Eaby-Sandy: Yeah. This comes up in Lung and Tumor Board all the time, is that you have a PET scan that's hot in those mediastinal nodes, but yet the pulmonologist says, "I went down, and I did a bronch EBUS and, I biopsied all of them and they were all negative." Is it falsely positive on the PET scan? Did the needle just not go in the right part of the lymph node? This is where multidisciplinary tumor boards are really important, and you have to take the patient into consideration.

If it's early stage, if those nodes aren't positive in the mediastinum, they should get surgery. But if they're lighting up like a Christmas tree on the PET scan, is there another reason? Was their blood sugar high that day, and that's why the PET lit up? There's so much that need to be assessed between radiology, the pulmonologist who did the procedure, did he feel confident when he did the procedure, that he got all of them? These are really challenging cases, and I think this early stage and stage III is where multidisciplinary tumor boards of utmost importance that these patients are discussed to determine why there might be discordant results.

Beth Gilbert: Right.

Beth Eaby-Sandy: I'm not going to say yes or no, of what I would do. I would say, it should be discussed with everybody and come to a decision.

Beth Gilbert: Yeah. What's new in oncology in the lung world? Early detection CT screening. To be eligible, you have to be age 55 to 77, asymptomatic, a 30 year pack/year history. Current smoker or you have quit in the last 15 years. In the guidelines, you can do it a little earlier, at age 50 with a 20 year pack history if you also have some additional risk factors. That could be, actually, a second cancer that's smoking related, or if you have a first degree relative with lung cancer, that also puts you in the bucket where you can get these CT screenings.

I just had a patient who, non-smoker now, but she had the history so she qualified. She was on her second year of the screening and she has two cancers on either side, two separate, different lung cancers that were found on the CT screening.

Beth Eaby-Sandy: She wasn't symptomatic, I'm assuming?

Beth Gilbert: No. Her last year scan was negative.

Beth Eaby-Sandy: Wow.

Beth Gilbert: She's completely asymptomatic.

Beth Eaby-Sandy: Plus, if she's a success story then she's [crosstalk] screening.

Beth Gilbert: Kind of, yeah. There's also trials looking to intraoperative glow, where the surgeon, they inject you with some sort of... Actually, that's all several different things they can inject you with that attach to cancer cells, so when the surgeon opens you up and they shine this light, theoretically, they can see cancer that they would not have known to take out prior. That's not in current practice at the moment, but it is being looked into.

Robotic surgery approaches, to help with the postoperative courses. [inaudible] robotic, and it's a little bit better postoperative, but there hasn't been any kind of change in any kind of survival with doing the robotic versus open surgery. But they're still working on things like that.

Principles of adjuvant chemotherapy, post surgery, for stage II and stage III. They're the ones that we're going to do surgery on, and think about adjuvant chemotherapy. Cisplatin-based is the pinnacle of what we would give these patients if they're considered to get the adjuvant chemotherapy. It improves

survival, decreases risk of relapse, and decreases risk of mets to the brain, with a adjuvant and backbone adjuvant chemotherapy when they are eligible. That's with completely resected, non-small cell. Concurrent radiation for N2 disease.

Beth Eaby-Sandy: Which, I found sometimes they do concurrent or sequential. Any thoughts on that?

Beth Gilbert: It does depend on how the ECOG status for the patient, that's one of the factors that... Sequential is-

Beth Eaby-Sandy: They do the chemo first, because the chemo has the most proven benefit for preventing recurrent disease. But then, if there was any N2 disease, they feel they should radiate the mediastinum as well.

Beth Gilbert: Yeah.

Beth Eaby-Sandy: Which, technically, they shouldn't have operated anyway if it was N2 disease, but it happens.

Beth Gilbert: That's another thing.

Beth Eaby-Sandy: But it happens.

Beth Gilbert: That's why it's important, staging. With the N2, they're very picky about who they'll take to surgery and it has to do with that N2-

Beth Eaby-Sandy: Node.

Beth Gilbert: Which we will get to. Adjuvant therapy in the resected non-small cell. Here are the studies that really, adjuvant chemo with cisplatin-based doublet establishes the standard of care with these patients with the completely resected non-small cell, because it increase five years survival.

Beth Eaby-Sandy: Yeah, you want to look right there. They're not huge gains, but they are gains, and they're statistically significant. Beth, is it worth it, do you think?

Beth Gilbert: I think so. If they can tolerate it. Patients want it. I would want it if it was me. I think any little gains, in lung cancers there's not huge gains, so whatever the little bit of percentages that we can get with whatever modality, and if you can tolerate it, we definitely recommend it.

They tried to add some things to the chemotherapy to improve it, on what the standard is. Adding bevacizumab did not improve any outcomes. Adding EGFR TKIs did not improve. Gefitinib and erlotinib were tested. There was a Chinese study that showed EGFR positive patients, that they did have a benefit from adjuvant gefitinib, but that was an outlier so I don't know about that one.

Immune check point inhibitors are being evaluated in phase 3 trials, they're all the ones that we know and love. Pembrolizumab, durvalumab, atezolizumab, and [olamab].

Here's our case study. This guy has a squamous cell lung cancer, stage IIIA. This was your patient, right?

Beth Eaby-Sandy: Yes.

Beth Gilbert: Yes.

Beth Eaby-Sandy: My actual patient.

Beth Gilbert: T2b, N2M0. He had a right suprahilar mass, molecular markers. He was PD-L1, TPS score of 2%. His staging MRI of the brain was negative, and as we know, everybody with a stage IB and up get a brain MRI. He had a PET scan, proven malignancy in the right suprahilar region was markedly FDG avid, and mildly increase uptake in an enlarged right paratracheal lymph node. Suspicious for nodal metastatic involvement. There was no metastatic disease.

There, the PET is lighting up in where they need to go, so they did a mediastinoscopy to that right paratracheal and it was positive. Squamous cell, PD-L1, also of 2%.

Beth Eaby-Sandy: If you note on the PET scan, it was mildly increased uptake and not enlarged. But when they did the med, it was positive. Again, good to actually stage the patient so he did not end up going to surgery.

Beth Gilbert: Here's some more information on him. He's a current smoker, smoked one pack a day for 40 years. Lives in a safe house, and his sister is supportive. He's got some cognitive deficits, he's bipolar, lacks some insight. He has hypertension, COPD. Not open to quitting smoking. In a wheelchair. Chronic joint pains, but walks around at home. This is the kind of patient, you don't get this patient every day with all of this, but you do see it a lot, for a lot of different issues that they have, social, as far as the lung cancer. How would you manage the patient, is what you got to start thinking of.

Are we talking about this?

Beth Eaby-Sandy: Yeah. I think you can go on. He will go on to get concurrent chemo/radiation because he had the N2 positive disease.

Beth Gilbert: I think we come back to him later one.

Beth Eaby-Sandy: Yeah, we will.

Beth Gilbert: Stage 3, surgery versus chemo/radiation. 3As, versus 3Bs. Controversial management strategies. Generally, standard of care in 3A disease is definitive, concurrent chemo/radiation without surgery. Although, surgery can be considered, but it would involve induction treatment with chemotherapy, or chemotherapy plus radiation prior to surgery. Proper staging, again, is paramount for these 3As.

Stage IIIB, never really surgical approach. Should always be concurrent chemo/radiation for curative intent, in general.

Beth Eaby-Sandy: I think this is where multidisciplinary tumor boards for stage III disease. If you get surgeons, [rad-oncs] and [med-oncs] in a room, they can fight stage 3 forever on how it should be

treated, surgery versus chemo/rads. They have an entire lung cancer conferences just on stage III lung cancer and how to properly manage it. I don't know any other thoughts.

I think in our institution we've come to an agreement that a single station, N2 node, which would make you a stage IIIA, but there was only one of them found, that we will often operate on that patient. If there are multiple N2 nodes, 3A is on the same side, so 3B means it's on this side. But, if you have a right-sided tumor, 3A is same side, there's multiple of them, it's likely that you're putting that patient at super high risk, and maybe doing a surgical approach is not the best thing for them. It may require a pneumonectomy, which is never good for morbidity. What do you hear in the talks?

Beth Gilbert: There is a lot of fighting... Not fighting back and forth, but trying to get the patient the best surgical option. It is in the guidelines, basically, for surgery that they try not to operate, or they don't think about operating if there's more than one N2 node and it's bigger than three centimeters. It's got to be small, it's got to be one. There will instances where maybe it's a younger patient, maybe it's this. That's why these multidisciplinary, if you're thinking about using surgery, chemo and radiation, that's definitely also in the guidelines that it should be discussed at a multidisciplinary atmosphere. Did you have a question?

Rashida Persinger: Just a quick question. [inaudible] institution, based on the fact that you all would offer surgery to, when there's just one N2 or lymph node involvement. Are you still taking into account the patient's clinical appearance, their comorbidities, their support system and so forth, like that, in making that decision in whether or not to offer that to a patient? Or is it highly encouraged to go to surgery, regardless of what some other issues that may impact the outcome?

Beth Gilbert: I think that's what the multidisciplinary is all about. Then you have to bring those things to light. Surgeon is just looking at, "Okay, I can do this." But if you really need to get the whole picture because... Yeah, all those comorbidities have to be in line. If they don't have good PFTs, then even if they had just one node and it was very small, then they wouldn't do anything. They wouldn't do it, because there is the option of just doing chemo/radiation.

Rashida Persinger: One last question. Have you seen patients that have come to you all, from the community, where they probably shouldn't have gotten that surgery because of those things? How would you address that with those patients once they come, and they've had surgery, probably should not have. Have multiple comorbidities, having multiple issues post surgery, if you are seeing that?

Beth Eaby-Sandy: You can't do anything.

Beth Gilbert: You can't do anything and you really just have to start at the point that you're at and then go forward. A lot of people want answers and they want... There's really nothing that you can do. You can only support them and just go forward and give them the best, whatever you could offer them.

To do chemo/rads or surgery plus chemo/radiation. This is a long list of studies here.

Beth Eaby-Sandy: Basically, the take home message is, these trials don't accrue well because patients think, "If there's a question, I should have surgery." They don't accrue, and we are not getting good results from them.

Beth Gilbert: Yeah. In general, just basically, surgery is very selective for 3A because surgery has comorbidity. I think that's what they have found in a lot of these studies. There was the P-value was not significant, meeting overall survival on longterm survival were pretty much the same.

Limited advances: an unresectable. Again, this is a nice timeline from the 80s, all the way until now. Beginning in the 80s, advances were made in the treatment of stage III, non-small cell lung cancer, with the integration of different treatment modalities. First, they added chemotherapy in front of the radiation, instead of just radiation alone. That improved survival.

Concurrent, chemo/radiation proved more effective than sequential use in these modalities, and cisplatin etoposide in 2002, was the doublet that was used for the chemo/radiation. That has been a standard for a long time.

Beth Eaby-Sandy: All the ones on the bottom did not add a benefit.

Beth Gilbert: Yeah, you can barely see them but they did try to add consolidation, docetaxel and then gefitinib maintenance. They tried vaccines. This was 2008 and 2014. In 2015, they tested higher doses of radiation, but the [60 gray] won out. Concurrent over sequential.

Tyler Beardslee: Just a note for that cisplatin etoposide regimen, it's actually different from the one we give in small cell. When you give it when concurrent chemo/radiation, it's kind of a complicated regimen. It's actually five days of etoposide.

Beth Eaby-Sandy: Yeah.

Tyler: The cisplatin phase one and eight [crosstalk].

Beth Eaby-Sandy: Tyler is making a really good point.

Beth Gilbert: Yeah.

Beth Eaby-Sandy: It's different than the way that we administer it with small cell, so the dosing is different.

Beth Gilbert: Most common regiments in stage III concurrent chemo rads. Again, usually daily fraction of radiation, 54 to 66 [gray], over six to seven weeks, Monday through Friday, no holidays, no weekends. Weekly paclitaxel and carboplatin are often used because of how well they're tolerated. But there's also cisplatin, or carbo and pemotrexed every three weeks. Of course, you don't give that to squamous histologies. The cis etoposide , here's dosing for that. The day 1/5 and day 1/8, two cycles. I think we're all probably pretty familiar with those.

Toxicity of these regiments, radiation can cause esophagitis, radiation dermatitis. Not so much, but visceral organ damage. The esophagitis, you have to work through that with the patient, but that does, obviously, get better. Can limit their intake and cause them to have to take pain medication, sometimes narcotics, sometimes they can get away without that.

Chemotherapy, the regiments can cause pancytopenias, neuropathy, hearing loss, nausea, vomiting. I think good renal function, you want to have good renal function because the cisplatin can really effect. Alopecia and several others.

Pneumonitis from radiation. Some studies show up to 25% of pneumonitis. It's generally later, months, two, three out, and out further. That's not an immediate thing that you're generally dealing with right there.

Again, the performance score, your ECOG is really important. When you're trying to determine what kind of treatment you're going to give them, can they tolerate it, chemo/radiation? Or do we have to do some sort sequential regiment, so that they can better tolerate it?

Most of these stage III's are unresectable, even if they're an A. Standard of care is concurrent chemo/radiation. We talked about the single station N2 node, the small tumor size. But what do we do after concurrent chemo/radiation? Prior to 2018, there wasn't much to do except for to follow them, put them in surveillance, get your scans every two, three months, and you had a high recurrence rate. In 2017, we had some improvements using immunotherapy to improve progression-free survival.

If we go back to our case study, he went on, and he did receive the carbotaxol with radiation for seven weeks. He tolerated it well, he finished. He had a post-CT scan and that showed no evidence of progressive disease in the chest. Interval marked decrease in the right perihilar mass, that shrunk a good bit for him. He had some relief with his right, mainstem bronchial tumor invasion. He had some persistent obstruction of the right upper lobe and some mucus plugging, which we tend to see a lot, this mucus plugging.

Probable associated lymphangitic carcinomatosis in the right upper lobe, stable to slightly improved. His mediastinum, it was overall stable, and he had some esophageal issues, some dysmotility. What do you do next with a patient, stage III, unresectable? They've received their chemo/radiation and prior to February of 2018, we just followed them. Now, we know we have durvalumab to give them, that showed progression-free survival improvement, and overall survival improvement.

Here's the study. Schema was a phase 3, randomized, double blind, placebo-controlled, multicenter international study. All these were unresectable, stage III, locally advanced. They had not progressed on their definitive chemo/radiation. There's all the other criteria. They started after the chemo/radiation, within 42 days they got 10 milligrams per kilogram every two weeks of the durvalumab for up to 12 months, versus placebo. They were randomized 2 to 1. Progression-free survival and overall survival were the primary endpoints.

Here is the graph showing how well durvalumab did over placebo. At 18 months the progress-free survival, you gained about 15 percentage points using durvalumab. It's pretty well tolerated. Of all the "mabs", I don't know, I see very little side effects from it. Here is our overall survival graft. Again, good improvement with durvalumab, where there was originally nothing to do.

Pneumonitis, it is a concern with all these PD-1 and PD-L1 immunotherapy grades, all grades, 34% versus placebo. Placebo had a lot, when I saw these numbers I was surprised.

Beth Eaby-Sandy: I'm glad we brought that up. I think 25% in the placebo arm, they're basically saying that 25% of patients developed pneumonitis just from radiation.

Beth Gilbert: From radiation, yeah.

Beth Eaby-Sandy: I don't think that's the case in our practice. I mean, it's maybe 10, 15%.

Beth Gilbert: I know. It was talking about all grades.

Beth Eaby-Sandy: I thought that was high.

Beth Gilbert: I thought it seems high.

Beth Eaby-Sandy: Yeah.

Beth Gilbert: I thought they both seemed high, from what I see.

Beth Eaby-Sandy: I think what happens on clinical trials is that people get short of breath and they're more likely to attribute it to whether it's placebo or drug, when it may have been a soft call. I don't know. I think the take home message here is that, adding immunotherapy right after you've finished blasting someone's lung with radiation didn't significantly increase rates of pneumonitis. All grades, it did increase by about 9%, but in that severe grade 3, 4, it was almost exactly the same. I think we can feel safe about that. I know that was my main concern, when durvalumab got approved, is like, "We're going to give this drug, but we already know it can cause pneumonitis to somebody who's already at risk for pneumonitis. We're going to see these huge rates of pneumonitis." But we really didn't, it wasn't that much more significant than it was in the placebo arm. I think that was comforting. [Rashida]?

Rashida Persinger: It's also all grades. Grade 1, are they really biopsied to confirm it? Or they just going by symptoms?

Beth Eaby-Sandy: Exactly. They're going by symptoms and radiographic findings, which they should be able to tell, but not always. That can masquerade as other things, and that's why I think they called it so high on the placebo arm.

Tyler Beardslee: Yeah, I think grade I is basic [inaudible] [crosstalk].

Beth Eaby-Sandy: It's asymptomatic, radiographic findings only. If you had a pneumonia that day that you got the CAT scan, it may look like a pneumonitis, and they may have called that. On a clinical trial, we're always more likely to just associate it with the study because we don't want to have any bias in saying it's not from the study. Take home message was, it wasn't that much more toxic, if at all, so that was good.

Beth Gilbert: Grade 3, 4, very close in percentage.

The PD-L1 status for this durvalumab trial, I think, Rashida, you had touched on that with the 25% designation. When they did that subgroup analysis just to look into the PD-L1 status, the greater than

25% PD-L1 status, they did do a little bit better. But again, that was just, they pulled it out just to take a look, it was empowered to do that.

Beth Eaby-Sandy: It was a random cut point of 25%. But what we had discussed in Rashida's talk was the negatives, the ones that were truly less than 1% or zero, technically in the subset analysis, did not have a statistically significant survival benefit. Now, again, that wasn't a prospective endpoint, so we don't use that as a reason to say, "No, I wouldn't give it to them." But they're less likely to benefit. So if there's any thought in your head that, that person shouldn't get immunotherapy, we're always looking for reasons in a negative patient. I wouldn't withhold it from them based on that subset analysis.

Beth Gilbert: Or, if they're having issues after starting the durvalumab, and you look back and you're like, "Their PD-L1 was not that high." Actually, I do have a patient who is symptomatic from the durvalumab, he's my only one. These patients really want to get it, they want the immunotherapy, they are doing it at all costs. This guy sits in my office and he barely breathes because he's like, "I don't want to cough." He doesn't want to alarm anything.

You see that a lot, where they don't want to tell you things because they want this immunotherapy because they want those extra... They see the commercials, that's what they see. They see the commercials and they think it's-

Beth Eaby-Sandy: The greatest thing ever.

Beth Gilbert: Yeah.

Beth Eaby-Sandy: But you're right. That would be the patient, if you looked back and saw a 0%, you might say, "I don't feel as bad about the risk/benefit of you actually getting that."

Beth Gilbert: Then you could really be like, "Hey, you know what?" Yeah. You can help the patient not feel bad about that, too.

Beth Eaby-Sandy: Mm-hmm (affirmative). Agreed.

Beth Gilbert: Pembrolizumab has a new indication as of April of this year for stage III, non-small cell, with a TPS score greater than 1%. That's brand new, that's really interesting.

Beth Eaby-Sandy: Yeah. The thing is, is that if you look at the indication, though, it's for patients who refused or were not candidates for concurrent chemo/radiation.

Beth Gilbert: That's the caveat. That's what it's approved for.

Beth Eaby-Sandy: Essentially, it's stage IV.

Beth Gilbert: You're treating a stage III like a stage IV.

Beth Eaby-Sandy: Exactly.

Beth Gilbert: For whatever reason, they can't get chemo/radiation, or they cannot get surgery, or they don't want either. Maybe you'll have a much older, who just wants, "I just want immunotherapy." They could actually get it with this indication now, as long as they have a TPS score of 1%.

Beth Eaby-Sandy: Right.

Beth Gilbert: Or greater.

Beth Eaby-Sandy: They say it's a stage III indication, but kind of, because really, you're treating them as a stage IV anyway.

Beth Gilbert: Yeah.

Beth Eaby-Sandy: I just want to be clear on that indication. There are not for patients post-concurrent chemo/radiation.

Beth Gilbert: Right.

Attendee: Are you extending [inaudible]?

Beth Eaby-Sandy: We are, because it's reflexed, so whenever they get diagnosed, we are automatically getting it. Now, Kristen brings up a good question, should we be? Beth?

Beth Gilbert: We can now, because there's the [inaudible].

Beth Eaby-Sandy: Yeah.

Beth Gilbert: I think so, because I think it's good to have, one, patients know that there's molecular that they should be having. Or, that they want to know every option that they can have. These patients recur so frequently, I would definitely do it. That's why we reflex it.

Beth Eaby-Sandy: I would completely agree. Their recurrence rates are high, so it's good to have that information, for it and when they recur. In the durvalumab case, you could possibly make... I don't want to say a treatment decision, but you could think of it in your arsenal of totally treating the patient of what their PD-L1 status is.

Attendee: Is Medicare paying for it, do you know?

Beth Eaby-Sandy: Yeah, I don't think-

Beth Gilbert: I haven't seen any issues.

Beth Eaby-Sandy: Yeah, I don't think Medicare would have an issue.

Attendee: [crosstalk] that what you re-biopsy?

Beth Eaby-Sandy: Not necessarily. If they recurred within six months, which is the most common time they would occur. It's lung cancer, it came back in six... You could biopsy, but.

Beth Gilbert: It depend... I think probably re-biopsy, yeah. But still, lung cancer is a heterogeneous, so maybe the sample you get, maybe it creates a treatment options, whether it's the PD-L status from the first one, you could still use, extrapolating. Even if the second one is not as, maybe it's just a sample. I still think it's got utility.

I'm going to go back. Our case study continued durvalumab and had no evidence of progression. His only toxicity was development of psoriasis on the arms and trunk of the body, which was treated with topicals and it wasn't bothersome. That's another, itching without a rash is a huge, huge issue with these drugs, I find. It's really bothersome for the patient, and we try all kinds of topicals. They slather all kinds of stuff all over their bodies and try antihistamines. I don't know if anybody has any good or better luck with anything.

Beth Eaby-Sandy: Or [crosstalk] therapy, [crosstalk] is going to be...

Beth Gilbert: Whoever invents something for that is going to be...

Beth Eaby-Sandy: Can you go backwards one, so I... There we go.

Beth Gilbert: Okay. Clinical pearls. In a nutshell, surgery in early stage of non-small cell lung cancer, stages I and II, is paramount. Rarely in stage III, but we talked about the exceptions. Chemo/radiation standard of care in stage III, non-small cell lung cancer in eligible patients and durvalumab for immunotherapy for one year, post-chemo/radiation improves progression-free survival, and overall survival in stage III patients.

Beth Eaby-Sandy: Okay. We'll ask questions again. If you guys have any questions, think of them, you can ask them.

A 60 year old gentleman has complete chemo/radiation for his stage III non-small cell lung cancer with weekly paclitaxel and carboplatin. He's here to discuss what would offer him the best survival advantage. You would counsel a patient on which option: immunotherapy for a year, post-concurrent chemo and radiation? Full dose consolidation chemotherapy followed by one year of immunotherapy? Stop with the concurrent chemo/radiation and go into surveillance imaging every three month, CAT scans? Full dose chemotherapy after the weekly chemo/radiation, and then go into surveillance imaging every three months? Or, you're still unsure? (silence)

Good. 100%. Did we get 100 again? Yes. Awesome.

Which drugs are approved for locally advance, non-small cell lung cancer after completion of concurrent radiation, when the cancer has not progressed? Is it pembrolizumab? Durvalumab? Nivolumab? Both A and B? Or, I'm not sure? (silence)

Good. Durvalumab is the answer, and why is IV not the answer? Anyone?

Attendee: [inaudible].

Beth Eaby-Sandy: Because it's not after chemo/radiation. Correct.

Beth Gilbert: [crosstalk].

Beth Eaby-Sandy: Pembrolizumab does have the approval and locally advanced, but it's only for patients who aren't eligible for chemo/radiation, hence treating them as in-curative, or stage IV as anyway. The only one that's approved at concurrent chemo/radiation is durvalumab.

Does anyone have any questions? Yeah?

Attendee: How often do you guys use the carbo etoposide regimen? That one is new to me [inaudible].

Beth Eaby-Sandy: It should be cisplatin etoposide. Beth, do you want to answer that? The cis etoposide, as opposed to paclitaxel and carboplatin, how often?

Beth Gilbert: We use carbotaxol a lot for that. Your question was-

Attendee: [inaudible] 10% that one-

Beth Eaby-Sandy: How often do you use cis etoposide in the [swag] regimen with radiation, as opposed to paclitaxel weekly, pac carbo weekly?

Beth Gilbert: We probably use pac carbo weekly, a lot more because a lot of the patients can't tolerate the cisplatin, or we have issues with renal or whatever. Do you get more?

Beth Eaby-Sandy: There's no head-to-head data between weekly pac carbo radiation versus etoposide cis radiation. If you look at the two studies separately, there is slightly better results with the etoposide cis and radiation, but it's really hard to get. It's five days etoposide and cisplatin on day one, day eight, and then you repeat it 20 days later. It's hard to get. We use it, I would say, about 10 to 20% of the time, and the other 80 to 90% is weekly pac carbo.

Again, they're stage III patients, so they often have bulky mediastinal disease, so their performance status isn't always awesome. Plus, their average age is in the 60s and they're heavy smokers. But if you have that really fit patient, a lot of times we will end up using a cisplatin-based regimen, whether it's etoposides cis or [pemo trex] and cisplatin, plus radiation. Both are really radiosensitizing regimens, as long as the patient can handle it. The other benefit you get out of that is you essentially get full-dose chemo with those.

The paclitaxel and carboplatin weekly, is sub-standard dosing. Remember, you're getting it weekly, but they're low doses, they're 45 milligrams per meter squared of paclitaxel, and AUC of two of carbo. Your body is never really seeing full-dose chemo, and the theory that's never been proven, but the theory on that is that if you have that rogue cell that's metastasizing, that we don't see on scans in a stage III setting, that you're never seeing full-dose chemo that could maybe eradicate it. As opposed to, if you got the etoposide cis or the pemotrexed cis regimen, they're full doses of cisplatin, so you are getting a better coverage of micro-metastatic disease that you don't see. But that's all theoretical and really, no study has every shown that consolidation full-dose chemo gave you a survival advantage.

None of those have gone to head-to-head with paclitaxel carbo weekly, so it's hard to say. But, if you just look at the separately, the survival rates are a little bit more in favor of the cisplatin if they can tolerate it. What you don't want to do is give it to somebody who can't tolerate it, and then they get only 50% of the chemo because they were so sick, and their counts were so bad. Then you're doing them a total disservice because they're just not getting all their chemo and radiation in.

It's a judgment call. I would agree with Beth, we mostly use weekly paclitaxel and carboplatin, because that's much easier to get all of your chemo/radiation in.

Tyler Beardslee: The other thing I would say is, I echo what you say about the very fit patient for the cisplatin etoposide, that's the only place I've ever seen it used. The other place is patient's that have [taxel] reactions.

Beth Eaby-Sandy: Yeah, that's a good point.

Tyler Beardslee: Switching to those other regimens. I actually had that this week.

Rashida Persinger: We don't [crosstalk].

Beth Eaby-Sandy: Rashida, you don't use the etoposide cis at all? Just the weekly pac carbo?

Rashida Persinger: Or the three week-

Beth Eaby-Sandy: Or the pemotrexed and cisplatin? Yeah.

Gary Shelton: Very good.

Beth Eaby-Sandy: Okay, thank you.

Gary Shelton: Thank you, Beth.

Beth Gilbert: Thanks.