Beth Eaby-Sandy: All right, so we're going to have a panel discussion. So, if I can have all of the speakers from today. We're just going to go over a couple cases, and I invite you guys in the audience, if you want to ask any questions, or have any cases of your own. We do have one case though, at least one, that was submitted prior to this. And then I had fabricated one myself, but we're happy to answer any cases that you guys would have about anything in lung cancer. We pretty much discussed A to Z today. So, we discussed toxicities of immunotherapy, if you have anything there that you want to discuss or ask questions of the panel, non–small cell, small cell, targeted therapies. All right, so let's get started. We know all of these things.

Okay, so this was submitted by one of our attendees.

"We saw a patient for a second opinion for metastatic non–small cell lung cancer. He came to us from an outside hospital, and had not had molecular testing done. We requested the tissue, but it was very delayed in arriving to us. Surprise. So in the meantime, the patient and the family wanted to start treatment, and they were anxious to start—it makes sense—and we had a first line trial available that included chemotherapy with immunotherapy. He proceeded and received cycle one. Of course, the week after starting we received the results, which indicated that he had an ALK mutation. Should we take him off of the trial and start him on an ALK inhibitor? One concern we have is reports that toxicity from the ALK drug could be worse, because the immunotherapy just had, what would you recommend?"

So, the only one that I'm aware of is osimertinib as an EGFR inhibitor. I'm not aware of an ALK drug causing toxicity after immunotherapy, though I think there's always a concern because it's a TKI. From a pharmacy perspective, Tyler, would you have concern of the ALK drugs post immunotherapy?

Tyler Beardslee: Like you said, I'm not aware of anything. I would probably run a quick lit search just to make sure I'm covering all my bases. But in this setting, with how strong the data is and the long-term survival with ALK inhibitors are, and the fact that he's on a clinical trial instead of a standard of care type of treatment, I would probably favor switching to an ALK inhibitor here like alectinib.

Beth Eaby-Sandy: Rasheda?

Rasheda Persinger: At our practice, my memory of what I bring is in standard of care. We've had patients that started on systemic therapy and when their mutation came back and they have a driver mutation, we always stop it. Our rationale for that is that at some point when the ALK or the EGFR, whatever progresses, we want to be able to go back to a chemotherapy base, and so with that thought process we would switch them.

Beth Eaby-Sandy: It's a really good point, and I would think from a clinical trial's perspective that this would kick the patient off.

Rasheda Persinger: Right

Entire Group: Right.

Beth Eaby-Sandy: Because now they have an ALK mutation, most frontline trials that are not targeted, you would think that, that would then make them ineligible for the trial. Boy, are you going to have to take a deviation.

Rasheda Persinger: But I am surprised that the clinical trial even allowed them on it without having that mutation.

Beth Eaby-Sandy: Without the confirmation. Yeah. Well, it depends on the study.

Tyler Beardslee: I think it would also be, I guess the one caveat I would say is maybe, I don't know, maybe they're close to getting a scan. You get a scan and they have some tremendous response.

Beth Eaby-Sandy: Yeah. Let's take the clinical trial out of this. Let's just say the patient was started on chemo IO without the data, and then the ALK came back. Maryanne, if it wasn't in a trial setting.

Marianne Davies: So we actually just had a case like this very similar. And the entire team decided that it was in the patient's best interest to switch them to an ALK inhibitor as well, given the data, and again, because of the clinical trial.

Tyler Beardslee: Yeah. The other thing that I think about, one of our doctors had this in his presentation, and it was talking a little bit about, We talked a little bit about this earlier, talking about sequencing of EGFR, doing this EGFR first, and then if they have T790M, maybe we can get some extended benefit. But he did a retrospective analysis on our patients and I think some crazy number like 50% of patients don't even make it to second line treatment. So, you don't want to risk that, especially if you know you have a very effective treatment upfront.

Marianne Davies: Yeah. So kind of similar to this. Well, not exactly, but we've had patients that have been on let's say a TKI inhibitor and then they've had some progression. We've added an IO to that and not taken away their TKI. So, I don't know the full data to that, but we've actually done that a fair amount with our faculty.

Beth Eaby-Sandy: After they've progressed on that?

Marianne Davies: If they've had some subtle progression or what not, we've added the IO and just kept the TKI blockade in there.

Rasheda Persinger: Now we've done it with chemo. So if we've had a patient that comes to mind already, good disease in the chest, but had some stable and even some response with the TKI, but some progression in the liver, we've added on the chemotherapy. Not the IO, but they're on the chemotherapy and [inaudible] stable disease in the liver since adding that but keep them on the TKI.

Tyler Beardslee: You should look back at your patients and write that up. Yeah.

Rasheda Persinger: I know

Beth Eaby-Sandy: So yeah, so I think that's a difficult case. The only other thing I would add is that, I'm assuming the patient's adenocarcinoma because they have ALK, and we know that pemetrexed actually works fairly well in ALK patients, but I still think that I would switch to the ALK inhibitor. They work so well in this population. They're so much less toxic and save your platinum based chemotherapy for later. Especially, if it's only cycle one. All right. Any audience cases or anything otherwise difficult? Ann?

Ann: Do you have a good resource for the [inaudible 00:00:05:45].

Tyler Beardslee: You were about to say something?

Beth Eaby-Sandy: The question is, does Tyler have a list of CYP3A4 interactions?

Tyler Beardslee: There was, gosh. It's, Oh man, I wish I had it on my head. There's a university that has a website and it has all of the CYP enzymes. It has all, every single one of them, I can't remember. I don't know why Pittsburgh is popping in my head. Pittsburgh, Baltimore or something like that.

Ann: You wrote that article of drug interactions [inaudible] ?

Tyler Beardslee: Yeah.

Ann: That was a good article.

Tyler Beardslee: Yeah.

Ann: But it didn't [inaudible 00:06:018]

Tyler Beardslee: Yeah. There is a university website. It's escaping me. I can't remember the name. I have it saved to my favorites tab. But yes, there is an...I don't know how many of you guys work on clinical trials. A lot of time in the clinical trials, this is where I found it, if you go down to the drug interaction section they reference this website. So, if you look in some of your trial protocols, go down to the drug interaction section, and you might luck out, and find this website that I'm talking about and is escaping me. I apologize.

Beth Eaby-Sandy: Okay. All right. Well, I'm going to move on to another case study that I kind of brought up and Mr. Oligo. So, case study of oligometastatic non–small cell lung cancer. Then Mr. Oligo, a 58 year old with adenocarcinoma, PD-L1 negative, no molecular alterations found with a good performance status presents with a four-centimeter right upper lobe mass, negative EBUS in the mediastinum. So, when they did the bronch EBUS, none of the mediastinum are positive. However, the MRI, the brain, found two foci of brain mets and a PET scan has one hot area in the right femur. That's generally asymptomatic. So you've got a guy that has a four centimeter right lung mass that we know is adenocarcinoma, no lymphadenopathy in the middle of the chest. But these MRI of the brain and a bone met. No, I, I always...do I have more to the case study? Is that my whole case study?

Rasheda Persinger: I thought you had a few more slides.

Beth Eaby-Sandy: Oh, I guess I even put in a treatment options. Are we going to record this? I just kind of threw this out there like, so 58 year old. So there's the story. So what would you guys do in this patient? I always laughed because oligo is one, but we consider it actually up to four to six sites of metastasis. You could still consider maybe a definitive approach. So what would you guys do—treat as metastatic disease? Technically it's metastatic, I mean its spread outside of the chest, treat with surgery, followed by stereotactic brain radiation and SBRT to the femur—treat with that, and in a year of immunotherapy treat with concurrent chemo radiation to the chest followed by immunotherapy. Anyone?

Marianne Davies: See again, it's not really oligo by my definition, but I mean they've got metastatic disease. The thing I worry about doing just the surgery is that you have nothing to follow. And I like to have at least some kind of a marker. You really can't follow the bone very well. So that's not going to be helpful. And I would definitely do SBRT to the brain lesions. I mean I think that that would definitely be my first choice. But there are some that would try to treat this definitively and go ahead with the surgery and maybe even our T to the bed if that, if that [inaudible 00:09:10],

Beth Eaby-Sandy: So my institution would do number two, we would do surgery on this case, the, because there's no nodal disease. Now if there was any thought of something in the mediastinum, then we would say no, absolutely not. But this was a case, this is a case for my institution. And they would consider surgery followed by the brain radiation followed by SBRT with a definitive curative approach and monitor the patient. Kristen.

Kristen: So if that's a four centimeter mass then you should give a post op [inaudible] ?

Beth Eaby-Sandy: Yeah. Yep. Well and then

Kristen: Two?

Beth Eaby-Sandy: Correct. So when would you sequence that in there? Would you, and these are all, you know, these are all questions for multidisciplinary tumor boards, but would you SRS the brain first without a lobe of the lung and then SBRT the femur? Like how would you sequence all of that? They technically have metastatic disease, so there's got to be a role for systemic therapy, right? With, would you call it adjutant chemotherapy at that point? Because then, and I'll tell you, I'll let you know about this patient. So the patient that went on to get adjutant chemotherapy, but we gave it with pembrilizumab because we felt the patient had stage four disease, which they did. We just technically treated all the sites of metastasis and then the patient went on to get immunotherapy and is in the midst of it is a year and a half into maintenance pembrolizumab and she would complete it at year two.

Tyler Beardslee: I think that approach makes sense.

Beth Eaby-Sandy: And then be done. But I mean that's an aggressive approach.

Tyler Beardslee: That's a very aggressive approach.

Beth Eaby-Sandy: There's no role for it. I mean are we considering it [inaudible] because all of the sites of disease are treated, but that's really a metastatic regimen.

Tyler Beardslee: Yeah, we've done this type of stuff on some of our younger patients. Who we are like maybe you know, maybe we cure this person. Who knows?

Beth Eaby-Sandy: I know it has been done. It certainly has been done.

Tyler Beardslee: This is, that's the only patient though that I think that has to play a role as well as you know, fitness of the patient and how young they are, how aggressive they want to be.

Beth Eaby-Sandy: And is there that abscopal effect with immunotherapy? You know, especially if you've done some radiation and maybe the immunotherapy is now going to add in a really empowered systemic effect. I don't know.

Rasheda Persinger: I think from our institution because we don't see a lot of the young people that have that excellent performance status where we more than likely would have done treatment for, and added to that, the radiation of the brain and kind of treat it like a stage three unresectable and then, but treat the area, we wouldn't have treated the femur because it wasn't symptomatic at that point. We probably would have just kept monitoring but definitely probably would have used two in those patients that are young that have great performance and we are trying to, you know, cure them. But more than likely we would have did four with SBRT to the brain.

Beth Gilbert: I would say your reaction, your face about, you know, treating them with all of that. And I have the same reaction when my, where I've had several cases like this where the physician that I work with was like, yeah. And I'm going through the case. I'm like, but this is a metastatic, they're, they have metastatic, their brain. They have, they have cancer in their brain [inaudible] and I'm like, why are we treating them like this? Or why are we in? So we've had several cases that also have prolonged effect by doing like cherry picking some of these things for small, like a bone lesion or a small brain lesion and treating them like they weren't metastatic.

Tyler Beardslee: There's a question about this in the guidelines too, right?

Marianne Davies: Definitely a fair amount of information as far as treating oligometastatic. And they do define it as a few scattered sites. And so as new sites pop up, they continue to recommend treating it as oligometastatic unless it's really big bulky disease. And that's what really shifts it. So if it's something that you can cherry pick as you say, then that's, that's typically the recommendation.

Beth Eaby-Sandy: Yeah. And I, and there's a lot of study now about having oligometastatic trials involving immunotherapy and seeing if we can get that effect on the metastatic sites that have abscopal effect on the metastatic sites, in addition to aggressively treating the primary. So I think this is something that we'll see more of back again. 15 years ago we would've never thought to, we'd be like, no way you have metastatic disease, good luck. And here's taxo carbo. [chorale laughing]

Marianne Davies: [inaudible] lung cancer with other diseases we might have done the cherry picking, but not with lung cancer.

Beth Eaby-Sandy: Yeah. Right. Yeah. Yeah. So, okay, good. So you all kind of agree. I don't think there was any more.

Oh yeah. So, so then I said, so let's say Mr. Oligo with the two brain mets, the one bone met the four centimeter mass has a positive EBUS with N2 disease. Now what would you do? And I think I had already kind of said this, but that's metastatic disease at that point. Once the N2 involvement, I mean that disease can be going anywhere. Would anyone disagree with that?

Well it already has, we forget.

Beth Eaby-Sandy: I know. I've, I can remember saying to some of the doctors like oligo. I know, right? One site, maybe two. I'll give you. It's just starting to be everywhere. Yeah. Okay. So I think that's the last one. Was there one more?

Oh, the voting.

Marianne Davies: So you must have thought you were treating this person as a stage three [inaudible 00:14:39].

Beth Eaby-Sandy: Okay. That's not the way we're treating them, but that's okay. So let's just say they were on durvalumab post chemo radiation. The TSH rises on the third month from a base. Oh yeah. Cause this was, this actually happened with a different patient of mind. The TSH rises on the third month from the baseline of 1.5 to 8.9 over a two week interval and the patient's asymptomatic, because I had an argument too with a certain physician about this. So the patient's not symptomatic. What would you do if their TSH, I mean it rose pretty quickly. Marianne?

Mariannie: Well first I would check the rest of their panel. And certainly a T4 level, and if the T4 level is normal then I would just continue to monitor them. And if they became symptomatic and certainly if they were over 10 or even up to 12 then I would probably start levo on them. I would base it on their T4. And that's how you, how you adjust your levothyroxin dosing anyway, is that you want to bring your T four to the middle range. So that's really your marker. It's not your TSH that you use after that point. So you need both of those numbers.

Beth Eaby-Sandy: Okay. All right. So that's good to know.

Beth Gilbert: Did the guidelines also say not to treat until it's over 10?

Marianne Davies: Well it's, if you're asymptomatic and your T4 is normal and just your TSH is elevated but it's still less than 10 then you don't have to treat.

Beth Gilbert: Oh okay.

Beth Eaby-Sandy: Yeah, I mean, and then the other concern here was that it was such a fast rise, but I see these TSHs go like this.

Marianne Davies: I would get the T4, add the T4 and then I would probably check them another like two. It depends on when they're coming in. If you're checking them at two weeks. So what are the, what drug are they on? Well,

Beth Eaby-Sandy: Their on durva.

Marianne Davies: So that's after two weeks. So just check them at their next dosing too, if their asymptomatic.

Beth Eaby-Sandy: Okay. Well let me see. Did I add any more questions?

Marianne Davies: It's a long plane ride home, wasn't it?

Beth Eaby-Sandy: It was like, Oh, and that guy. Okay. Okay. So any other questions from the audience cases?

Tyler Beardslee: I had one small thing I wanted to add.

Beth Eaby-Sandy: Yes, please do.

Tyler Beardslee: One thing that I've done in a couple of my patients, just because this is like a, it's not something that's going to happen a lot of times, but in your HER2-mutated patients, you could also use ado-trastuzumab emtansine. You're not going to hear me say that again, which is a HER2-directed antibody, which has a payload of emtansine, which is like a super duper powerful anti-microtubule drug. They use this in breast cancer.

Tyler Beardslee: So yeah, that drug's an option. There's this small phase two study with like 20 or 30 patients and it had like a response rate of like 40% we've done it in a couple of our patients and had decent results

Marianne Davies: And us too, we've had two patients with that and we use that drug and it's been pretty amazing.

Tyler Beardslee: Yeah.

Marianne Davies: I was going to mention that during your time.

Beth Eaby-Sandy: Do you think that they'll go for an approval?

Tyler Beardslee: I don't. I'm not sure. I don't know if they're studying it or not in bigger trials.

Marianne Davies: It's a small population.

Marianne Davies: And we haven't had a problem getting it approved, so I'd have to look at the basket trials too, to see if it says included.

Beth Eaby-Sandy: Okay.