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https://reachmd.com/programs/cme/panel-discussion-patient-selection-emerging-studies-and-strategies-in-es-sclc/16489/

Released: 11/30/2023
Valid until: 11/30/2024
Time needed to complete: 1h 22m

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Panel Discussion: Patient Selection, Emerging Studies and Strategies in ES-SCLC

Announcer Open:
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Dr. Leal:
Hello, I'm Dr. Ticiana Leal. I'm an Associate Professor and Director of the Thoracic Medical Oncology Program at the Winship Cancer Institute of Emory University. And I'm joined today by my colleague, Dr. Jacob Sands. Welcome.

Dr. Sands:
Thank you. Happy to join you. I'm Jacob Sands, Thoracic Medical Oncologist from Dana Farber Cancer Institute.

Dr. Leal:
And in this episode, we'll talk about patient selection for second-line therapy, specifically with lurbinectedin, and also discuss emerging combination strategies for second-line, extensive-stage small cell lung cancer.

So, let's start with our first topic. Currently in second-line, we have two approved FDA agents, topotecan as well as lurbinectedin. And let's talk about which patients are most suitable for treatment with lurbinectedin, and how you view platinum-sensitive or platinum-resistant disease. How does that impact your choice of second-line therapy?

Dr. Sands:
Well, I'll admit that, broadly, I tend to use lurbinectedin in general over these other lines. Topotecan is not something I commonly utilize. As we discussed in our other episodes that people can go back to for more details on that, but I find irinotecan to be better tolerated. And so, I'd prefer irinotecan in general, anyway. Lurbinectedin is often my second-line standard-of-care option in patients not being enrolled into a clinical trial. But I'll just take a moment to highlight clinical trial enrollment is a really important aspect of the treatment courses. So lurbinectedin would be my second-line choice, whether they're platinum sensitive, platinum resistant, that is more consistent second-line choice for me. Some outliers, as we've highlighted in some of our prior episodes, is patients who have had platinum/etoposide with radiation, and then later on have recurrence or progression, then I may do platinum re-treatment, while incorporating a checkpoint inhibitor in that setting.

Dr. Leal:
Yeah, and I think another important topic is the topic of brain metastasis. For patients with small cell lung cancer, especially in second-line where, you know, we do see over the course of the disease, high rates of brain metastasis or brain metastasis recurrence, the use of lurbinectedin in patients with brain metastasis, I think is a topic of great importance.

Typically, you know, in my own clinical practice, I tend to use radiation as sort of the main way to treat the brain metastasis and have increasingly used stereotactic radiation for selected patients in conjunction with a multidisciplinary evaluation with a radiation oncologist. But we don't have a whole lot of data with lurbinectedin in brain metastasis. What is your approach in these cases?

Dr. Sands:
Well, I frankly don't expect a lot of efficacy from lurbinectedin, but we don't really have any data to go from. So, it's not a line I would use when I really need intracranial treatment. But related - somewhat related to that, if someone has intracranial progression only, and radiation can be done, then I'd radiate that and continue them on their checkpoint inhibitor. And I highlight that because I do have some patients with very prolonged ongoing disease control. From the best case is someone right now, who's really 4 years out from getting radiation to her brain that still has not needed a second-line therapy, a second-line systemic therapy. So, I think it's important to really consider brain progression separately.

But Dr. Leal, what about in patients with a somewhat borderline functional status, are there regimens that you prefer in that setting? And where is your line in consideration on when you'd go to a next line therapy versus not offering further options?

Dr. Leal:
Those are great points. Most of the studies included only patients with performance status of 0 to 1. In the lurbinectedin study, they did include patients with ECOG performance status 2. So, we do have data from the lurbinectedin phase 2 trial of use of lurbinectedin in patients with performance status of 2. We've also seen exploratory analysis of both the phase 2 trial, as well as ATLANTIS, looking at patients 65 and older.

So, I think for patients that are motivated that have good performance status, or that are motivated and may have performance status of 2, but have good social support, I think it is reasonable to have an informed decision-making discussion and I think lurbinectedin has some data to support the use in patients that are older and patients would performance status of 2.

I think introducing palliative care is really important and I tend to introduce it early and I tend to have palliative care follow the patient along with us. I find them to be very helpful as an extra layer of support, not only in symptom management but in decision-making as well.

So those are, I think, my thoughts. If lurbinectedin has been used and the patient still is motivated to receive additional therapies, I tend to use the weekly regimens, irinotecan or paclitaxel. And again, the choice between those two is really if you're trying to avoid certain toxicities, for example, with irinotecan diarrhea, with paclitaxel neuropathy. I tend to sort of use irinotecan more frequently, and that has been well tolerated when you use the weekly strategy.

Dr. Sands:
Now, Dr. Leal, across all of our episodes, we've really highlighted the value of clinical trials. And there are a lot of trials going on. What are some of the emerging combination trials? So, we've mentioned a lot with lurbinectedin, but what are some of the combinations of lurbinectedin that you'd like to highlight in managing second-line and beyond?

Dr. Leal:
So, I think a really awaited trial is the IMforte trial, looking at the use of lurbinectedin plus atezolizumab, versus atezolizumab alone in patients with small cell lung cancer after completion of induction. So, this is now investigating the addition of lurbinectedin to atezo maintenance and looking at outcomes.

The second combination that I'm very interested in seeing results is the confirmatory phase 3 LAGOON trial, looking at now lurbinectedin monotherapy or lurbi plus irinotecan, versus investigators choice of chemotherapy, in patients with small cell lung cancer progression following a prior platinum-containing regimen with or without immunotherapy, here with the primary endpoint of overall survival.

And there are many other combinations investigating lurbinectedin with other agents. We have a phase 1 trial here at Emory, which is an IST led by Dr. Kristen Higgins, investigating lurbinectedin plus radiation, here with the primary endpoint of safety, looking at some efficacy endpoints as well.

And then we saw some interesting data ESMO about the combination of lurbi plus pembrolizumab in a population that had not previously received immunotherapy, which did show some interesting efficacy outcomes and tolerability. What are your thoughts on that data?

Dr. Sands:
Well, you know, I've highlighted the importance of a checkpoint inhibitor in those who have not previously gotten one. And so, in someone who has not had a checkpoint inhibitor, I want to incorporate it, I have used pembrolizumab as monotherapy at times. And so, in those - it's not common, but in those cases, to then have this combination and have it as an option, I found that quite interesting as well. I really liked that data.

Dr. Leal:
Yeah. Other strategies that I'm excited about include investigating the use of the bispecific T-cell engagers. We saw updates from the

phase 2 trial at ESMO of tarlatamab in patients previously treated, with extensive-stage small cell lung cancer, that showed really encouraging results with, you know, safety that's kind of held up in terms of cytokine release syndrome being the most common side effects, the majority grade 1 and 2 in nature.

And then we also saw other T-cell engagers, now TriTE's also in the mix with early phase data, similarly kind of tracking with similar early efficacy and similar sort of safety issues with the cytokine release syndrome being the main one, but manageable.

And then lastly, the antibody drug conjugates are also I think, really emerging as an interesting strategy. We saw the results of I-DXd, an ADC targeting B7-H3, demonstrating really promising results with response rates in the order of 58%, with safety profile that is pretty manageable.

Any other thoughts about emerging strategies that you're excited about?

Dr. Sands:
Well, you've highlighted some really important classes, and the fact that there are so many different drugs to discuss is what's so exciting. I mean, now we could go on for much longer now on all of these different emerging therapies. And that's a fairly new thing in the small cell lung cancer realm to have so many different topics for discussion.

Unfortunately, that's all the time we have for today. But I want to thank our viewers for joining us in these episodes on small cell lung cancer. If you haven't caught our prior episodes, please go back to this for more information on all of this.

And with that, thank you, Dr. Leal, for joining me for all your insights in the management of small cell lung cancer.

Dr. Leal:
Thank you.

Announcer Close:
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