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Recent Advances in Melanoma from the 2022 European Congress

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Dr. Luke:
Hi, I'm Jason Luke from the UPMC Hillman Cancer Center in Pittsburgh, Pennsylvania. I'd like to thank you for joining us today as we review the high impact melanoma abstracts from ESMO 2022. And joining me today is Dr. Zeynep Eroglu, from the Moffitt Cancer Center. Thanks for joining me today.

Dr. Eroglu:
Thank you for having me.

Dr. Luke:
So we'll jump right in and start discussing these abstracts. And I think there's no question that at ESMO this year for melanoma, the biggest deal of the big deals was the SWOG 1801 neoadjuvant trial, of presurgical pembro followed by adjuvant pembro versus adjuvant pembrolizumab alone. So, Dr. Eroglu, do you want to speak to the trial design quickly and what the results were, and how you think this impacts practice?

Dr. Eroglu:
Yeah, absolutely. So, S-1801 was a large study that was looking at patients with resectable stage 3-B to stage 4 melanoma post who are essentially candidates for surgical resection. And the patients were randomized to either upfront neoadjuvant therapy which meant they received three cycles of new adjuvant pembro followed by surgery, followed by adjuvant pembro. Versus upfront surgery, followed by one year of adjuvant pembro, which is essentially what we do now with standard-of-care adjuvant anti-PD-1 therapy. And the primary endpoint of this study was event-free survival. So that was basically a combination of either disease progression, disease recurrence, toxicity, death, or failure to start adjuvant pembro. So, a combination of all of these. And the, what the investigators found, led by Dr. Patel, after enrolling about 345 patients, was that the two-year event-free survival was 72% in the neo-adjuvant cohort versus only 49% in the adjuvant pembro cohort. So definitely a significant response.

Dr. Luke:
And so it seems in talking with some of our colleagues that were there already petitioned the NCCN to endorse this strategy as standard practice. So how do you think these results really impact in what you guys are going to do at Moffitt like on a daily basis?

Dr. Eroglu:
Yeah, so I think currently with NCCN neoadjuvant treatment is put in as a "can consider" type of recommendation for patients with

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clinically lymph node-positive disease. But my guess would be you know following the results of S-1801, it will become a much stronger recommendation for both stage three and four melanoma. So, I think it we'll see an increased utilization of neoadjuvant immunotherapy in melanoma.

Dr. Luke:
Yeah, and I would emphasize that just as much. I think this is now probably a standard approach for patients that have clearly resectable disease but a lot of questions remain, is pembro alone enough, combination I O, how many doses all these kinds of things really matter. So, let's move on to the next abstract which is another really important one I think which was the late-breaking abstract number three, randomizing patients to get TIL therapy versus ipilimumab for PD-1 refractory disease. So, you want to comment on that study quickly and how you think it'll impact on practice?

Dr. Eroglu:
Absolutely. So, this study showed a significantly improved, progression-free survival in patients who received TIL therapy, versus ipilumumab therapy. I think 7.2 versus 3.1 months. So, these were patients who had gotten one prior line of systemic therapy, which for most of them was PD-1 therapy either in the AGEN or metastatic setting. I think that, you know, oftentimes we still tend to utilize Alu map-based regimens, or you know sometimes targeted therapy in patients with BRAF disease. But I think this study kind of makes us question, you know should we actually consider Til therapy earlier, as opposed to waiting until patients have gone through multiple lines of therapy and kind of maybe looking at it as a last resort. I would emphasize though this study did look at a group of patients with better outcomes. You know, they limited to age up to 75, PS of only zero one, LDH less than two times upper limit of normal. So, I think that enables impact, you know the good outcomes. But I think there's definitely a role for, you know considering Til therapy earlier on.

Dr. Luke:
And I thought it was important to emphasize these data as well because in the United States we've had clinical trials of a commercial Til product called Lifileucel. Which look interesting and very possibly could get approved in the coming year. And these data can help to inform how we might use that product if it does get approved. So having discussed that, let's move on then to discussion of the Immuned trial. This was a neoadjuvant trial for stage four resected disease looking at combo IO versus PD-1. You want to comment on this and how this has changed your practice.

Dr. Eroglu:
But I think what's interesting in this study is looking at the traditional EP NIVO, EP three NIVO one, four doses in the adjuvant setting versus adjuvant Nivolumab in stage four patients, which you know the investigative showed a statistically significant difference with improved relapse re survival with combination immunotherapy in stage four. So, I think there may be a role for combination EP NIVO, with the standard dosing in stage four patients post-surgery.

Dr. Luke:
Yeah, and I think that's the really important point. And in my practice for patients who have resected stage four disease I do use NEVO plus IPI and not just PD-1 monotherapy for the reasons that you kind of just outlined. So, the final study I think is an important one to wrap with. This was the update on the Secombit trial and this was the study of immunotherapy first then BRAF, or vice versa or the sandwich.

Dr. Eroglu:
So I think with Secombit also, you know, we can see that the starting with immunotherapy and then reserving BRAF inhibitor at progression did lead to superior outcomes in progression-free survival versus starting with from BRAF inhibitor therapy. The study did have a sandwich cohort, but you know from what I saw that did not seem to make any differences at least thus far with regards to outcomes. So, I'm not sure there's necessarily, you know strong benefit in doing that standard approach, versus just starting up front with upfront EP NIVO.

Dr. Luke:
And that was the take home that I got as well is, that really, it's immunotherapy first before BRAF and melanoma. And that is in contrast with say what we see in lung cancer for targeted therapy. But I think that, like you said, I think that that is something in our practice that already changed what we need to emphasize for the community because we do still see patients treated with BRAF inhibitor in the frontline sometimes. So, with that I'd like to say thanks for listening to us here, review the abstracts from ESMO this year a lot of really high impact studies and we'll look forward to next year.

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