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Phase II Study SECOMBIT (Sequential Combo Immuno and Target Therapy Study): 4-Years OS Data and Preliminary Biomarkers Evaluation

Announcer:
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Dr. Ascierto:
My name is Paolo Ascierto, I'm a medical oncologist. I'm the head of department of Skin Cancer and Cancer Immunotherapy at the National Cancer Institute of Naples, Italy. And at the ESMO 2022, on behalf of all the other investigators from the SECOMBIT study, I reported an update with 4 years overall survival data in some preliminary biomarkers evaluation of the SECOMBIT study. The study about different sequence in metastatic melanoma patients, BRAF mutated.

You know, the SECOMBIT study is a randomized phase II study, which explored the difference between three different sequences. The first sequence, with the combo targets first, with Encorafemib and Binimetinib given as first, and then in case of progression, the combination of Ipilimumab and Nivolumab at the classical 3 mg/kg dosage. The second sequence, with the combo immunotherapy, is first, and then in case of progression, Encorafenib, and Binimetinib. And then, the so-called "sandwich arm" that is to say, short induction, 8 weeks with Encorafenib and Binimetinib, then switch to immunotherapy with Ipili and Nivolumab at response. And then, in case of progression, again target therapy, with Encorafe and Binimetinib. We reported the data at the database lock 30th June with the medium follow-up of 43 months. And we report the data of the total progression for survival for years and also the overall survival rates at 4 years in preliminary biomarkers data.

Here, the patient disposition of the 209 patients randomized in different arms.

And, as you can see, looking the 4 years total progression-free survival, that is to see the progression-free survival I and the progression-free survival II the arms where immunotherapy was given as first, went better of arm where target therapy was given as first. With more than 25% of advantage for the arms B and C. Even there's a ratio exploratory, that's the ratio were significant. In terms of overall survival, the results was still in favor of the arms where immunotherapy was given as first. But the gap was a little bit lower. But still, we can say that the arms where immunotherapy was given first, went better. Looking the subgroup analysis of the patients with normal elevated LDH. It's interesting to see in the group with the elevated LDH, and here you can see the total progression-free survival on the top and then the overall survival. The sandwich arm went better in patients with elevated LDH, and also in the patients with high tumor burden. Still, the patients who performed, who received immunotherapy first went better, compared to arm A.

We also did an analysis about, this is a preliminary analysis about biomarkers. We looked at the inflammatory cytokines and the target sequences NGS. We evaluated between 80 and 90 patients. So, the analysis is still ongoing with the remaining samples.

And interestingly, if you look the tumor mutational burden, high TMB was better in arm A and B. Interestingly in arm C, no difference. Probably because this arm was more affected by target therapy. Another interesting data is about the JAK mutation. As you can see, the JAK wild-type patients, more or less, no difference among different arms. While for the JAK mutation, it's interesting to see that the patients in arm B, JAK mutated, went all better. With 100% of patients total progression-free, and still alive after 4 years. So, of course the limiting, this analysis, it's that this is a small number of patients we see with additional markers.

And finally, interferon-gama cytokine, not signature. And no difference in arm A and B, between low and high interferon-gama cytokine. But it's interesting in arm C, to see the patients with low interferon-gama cytokine went better. So, we still don't know the why. Of course, with the further analysis, we will look at this.

So, in conclusion, with a medium follow-up of 43 months, the total progression for survival and overall survival in 4 years was convenient better in the arm B and C, with immunotherapy first. Looking to the subgroup analysis, in patients with the elevated LDH, and with more than 3 metastatic sites involved. But still, the arms where immunotherapy went better, was good. Interesting preliminary biomarker analysis for the elevated TMB, JAK mutation, and interferon-gama cytokine. I have to say that biomarkers side are still on progress, and ongoing with a larger number of samples. And of course, the study's ongoing to evaluate the long-term outcomes.

I'd like to thank all the people work to SECOMBIT, and the investigator, and of course, thank you for your attention.

Announcer:
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