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Adjuvant Nivolumab Alone or in Combination with Ipilimumab Versus Placebo in Stage IV Melanoma with No Evidence of Disease: Overall Survival Results of IMMUNED, a Randomized, Double-Blind Multi-Center Phase 2p DeCOG Trial

Announcer:
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Dr. Schadendorf:
Hello everyone. I'm going to talk about The IMMUNED study, which is a treatment of Adjuvant Nivo alone or in combination with Ipilimumab versus placebo in Stage IV Melanoma with no evidence of disease, and I'm going to report the final overall survival data of that study which was conducted in Germany.

So, the background of the study is that checkpoint inhibitors and targeted therapies are approved for adjuvant treatment of high-risk resected melanomas. We have one drug which is approved, Nivolumab in Stage IV Melanoma with no evidence of disease and we have reported the primary endpoint of the study of IMMUNED two years ago, reporting that relapse-free survival of NIVO IPI and also Nivo versus placebo was improved. Now we are reporting the final relapse-free survival and first and final OS data with a median overall survival follow-up time of 49 months.

The study design is shown on this slide. You see three-arm study, 1:1:1 randomization. NIVO IPI was done in the induction phase with appropriate placebo controls. The same with Nivo over the first 12 weeks are in gray, Nivo matching placebo which was given, and then maintenance was given with Nivo in arm A and B, and Nivo matching placebo in the placebo arm. Study enrollment was between September 2015 and November 2018. And we have seen already and reported two years ago that the median time on treatment was quite different between the Nivo placebo between 22 to 24 weeks on treatment versus 6.5 weeks for the dual checkpoint blockade so that almost 50% of the patients prematurely terminated treatment in the NIVO IPI treatment arm.

Nevertheless, when we look now at the final RFS analysis, we see that there is a statistically significant benefit of NIVO IPI versus placebo and NIVO IPI also over Nivo, and Nivo was also statistically significant superior to placebo alone and the hazard ratios ranging between 0.25 and 0.6. Median relapse-free survival time ranges between six to 12 months placebo and Nivo, and not reached after 49 months for NIVO IPI at this time point.

This translates also now in the secondary endpoint, we are reporting overall survival in all patients. Of these 167 patients in the intention-to-treat population, only 36 events have occurred at this point in time, but nevertheless, you see a nice separation which shows a clear benefit for NIVO IPI with a four-year survival rate of 84% versus placebo, which is after four years, 63%, and Nivo mono, 73%. Statistical significance is present for the NIVO IPI versus placebo. The others show also impressive overall survival data and hazard ratios, but they are not statistically significant at this point in time because of the low event rate we have at the moment.

When we look what is influencing overall survival, we have addressed what was given as first subsequent systemic treatment in all our randomized patients. Only 18 patients progressed in the NIVO IPI arm. Most of these patients got treated either if their BRAF mutant was targeted therapy or received a checkpoint. Again, it's very similar. In the Nivo arm here, 36 patients relapsed. Most of the BRAF mutant patients got targeted therapy. Interestingly, in the placebo group we have possible crossover. However, only 19 patients crossed truly over from placebo to Nivo monotherapy. 19 patients opted for that, and additionally, 23 patients crossed over. Outside the protocol, the majority of those also received a checkpoint blockade.

So, at the end, I think we have to conclude, this is the first prospective randomized placebo-controlled trial in Stage IV Melanoma with no evidence of disease. After a median follow-up of 49 months, we see statistically improvement of relapse-free survival versus placebo of Nivo but also NIVO IPI, which is quite profound. In addition, we see also a NIVO IPI statistical significant improvement versus a Nivo monotherapy. And this translates also in overall survival benefit with four years survival rates of 84 for NIVO IPI, 73% for Nivo mono, and 63% for placebo. However, subsequent PD-1-based therapy in placebo patients is most likely impacting overall survival comparison between Nivo and placebo. This study reports for the first time data in Stage IV NED after surgery and radiotherapy and supports the use of dual checkpoint blockade in this patient population. Data have been published in Lancet Online September 10th. Thank you for your attention.

Announcer:
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