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Session B. Melanoma and skin cancer

B08 CheckMate 067: a phase III randomized double-blind study of nivolumab (NIVO) monotherapy or NIVO combined with ipilimumab (IPI) versus IPI monotherapy in previously untreated patients (pts) with advanced melanoma (MEL)

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Background: Results from a phase I study in MEL pts suggested complementary clinical activity between NIVO (a programmed death-1 [PD-1] immune checkpoint inhibitor) and IPI (a cytotoxic T lymphocyte antigen-4 [CTLA-4] checkpoint inhibitor), and was used to determine the combination dosing for phase III trials. Combination treatment resulted in a higher frequency of pts with tumor volume reduction and unprecedented rates of 1-yr survival (94%) compared with data from other NIVO (73%) or IPI (47%) trials in a similar population. The combination resulted in a safety profile with similar types of adverse events (AEs) as IPI alone, albeit a greater frequency in some cases. This phase III double-blind study evaluates the contribution of monotherapy components to the combination activity and safety, in order to best characterize this regimen in pts with either BRAF wild-type or V600 mutation-positive advanced MEL.

Methods: The co-primary endpoints are PFS and OS in the NIVO + IPI combination group or NIVO alone compared with IPI. Secondary objectives include objective response rate (ORR) and PD ligand-1 (PD-L1) expression correlated with efficacy outcomes. Treatment-naïve pts (N = 945) with metastatic or unresectable MEL were randomized 1:1:1 to receive NIVO 3 mg/kg every 2 weeks (Q2W) + IPI placebo (PBO) Q3W, or NIVO 1 mg/kg Q2W combined with IPI 3 mg/kg Q3W for 4 doses followed by NIVO 3 mg/kg Q2W, or IPI 3 mg/kg Q3W + NIVO PBO Q2W for a total of 4 doses followed by NIVO PBO Q2W until progression or unacceptable toxicity. Pts were stratified by PD-L1 status, BRAF status and M Stage. Tumor assessments first occurred at 12 weeks after randomization, Q6W for 49 weeks and Q12W thereafter. The co-primary endpoint of PFS will be reported with a median follow-up greater than 12 months based on a planned data analysis in early March 2015. Additional endpoints will include ORR, duration of response, tumor burden reduction and PD-L1 correlation with efficacy across prospectively defined pt subgroups. Safety will be reported in all treated pts and will include the incidence and resolution of select AEs.