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Randomization to adjuvant nivolumab or ipilimumab + nivolumab based on pathological response to a single dose of neoadjuvant nivolumab in stage III melanoma

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Background

Melanoma patients (pts) who do not have a pathological response to neoadjuvant anti-PD-1 have a poor prognosis; intensifying adjuvant therapy based on pathological response after a short course of neoadjuvant therapy may improve outcomes and reduce toxicity.

Methods

In this investigator-initiated study, pts with clinical stage III melanoma received one dose of nivolumab (480 mg) followed by surgery 4 weeks later. Pts with a major pathological response (MPR), including pathological complete (pCR) or near complete (<10% viable tumor; near pCR) response received adjuvant nivolumab for up to one year (Arm A). Patients with less than a MPR were randomized 1:2 to either adjuvant nivolumab (Arm B) or adjuvant ipilimumab (1mg/kg) plus nivolumab (3mg/kg) every 3 weeks for 4 doses followed by nivolumab (Arm C). The primary endpoint was 1-year recurrence-free survival (RFS). Secondary endpoints included overall survival (OS), MPR rate, and safety.

Results

70 patients were enrolled from 2019-24. 66% men. 54% stage IIIC/D by baseline clinical nodes. All underwent resection. 23 pts had a MPR (33%; 20 pCR, 3 near pCR). 7 patients had pPR. At a median follow-up of 21.4 months, the estimated 1-year RFS rate was 100% for pts treated per arm A, 55.6% (22.6% – 77%, 95% CI) for Arm B and 61.5% (40.3% – 77.1%) for Arm C. The median OS was 21.4 months in all patients and was 22.9 in Arm A. 9 pts (37.5%) in Arms A and B, and 15 pts (62.5%) in Arm C had grade 3/4 treatment-related adverse events.

Conclusions

Patients who had a MPR after a single dose of neoadjuvant PD-1 blockade have a high RFS (100%) and OS (100%). MPR was prognostic of RFS (log-rank p=0.002) and OS (log-rank p=0.019). Pts without a MPR had a numerically higher RFS when treated with ipi/nivo than with nivo alone, which was not statistically significant. This study demonstrated that adaptive adjuvant therapy based on pathological response is feasible. Longer follow-up will confirm whether or not there may be any benefit of immunotherapy escalation in the adjuvant setting. Translational studies are under way to evaluate the effect of different adjuvant therapies on immunophenotype of melanoma-specific CD8 T cells and across cell types.

Clinical trial identification

NCT04013854.

Legal entity responsible for the study

University of Pennsylvania.

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Disclosure

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