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Enfortumab vedotin (EV) plus pembrolizumab (P) for refractory advanced melanoma: Primary results from the PLUG-IN GEM 2301 trial

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Background

Melanoma has high NECTIN-4 expression levels. EV plus P, has demonstrated impressive efficacy in other tumor types. This study aims to evaluate the efficacy of EV+P in advanced melanoma after progression (PD) to standard treatment (Tx).

Methods

PLUG-IN is a phase 2, single-arm, multicenter clinical trial for patients (pts) ≥ 18 years with locally advanced/metastatic melanoma, ECOG 0-1, and measurable disease per RECIST 1.1, regardless of NECTIN-4 expression. Pts were divided into BRAF-native post-immunotherapy (IC) (C1) or BRAF-mutated post-IC and targeted therapies (C2). Uncontrolled brain metastases and systemic corticosteroids were excluded. EV was given at 1.25 mg/kg on days 1, 8, 22, and 29, and P at 400 mg on day 1 of each 6-week cycle. The primary endpoint was confirmed objective response rate (ORR). The study aimed to enroll 60 pts, assuming a historical ORR of 15% (H0) and a potential increase to 30% (H1), $\alpha=0.05$, power 80%.

Results

At data cutoff (Apr26) sixty pts were included, 53 evaluable for efficacy, with a median age of 58 years (range 18-87), most female (51.7%), acral (20%), mucosal (16.7%). Metastases were present in lung (43.3%), liver (28.3%) and brain (10%). Forty-five were BRAF-native (C1) and 15 BRAF-mutated (C2), included after PD to ≥ 2 prior systemic therapies in 46.7% and 73.3%, respectively. Response confirmation is ongoing; confirmed ORR: 17%. The best response rate (BOR) was 28%, with two (3.8%) complete and thirteen (24.5%) partial responses. The BOR was 20.0% in C1 and 40.0% in C2. The BOR was 23.3%, 50%, 12.5% in cutaneous / acral / mucosal. EV was administered for a median of 3.0 months (95% CI: 2.0-3.7) and P for 2.7 months (95% CI: 1.4-3.0). Tx is ongoing in 32 pts (53.3%) and was discontinued due to PD (31.7%), death (8.3%), toxicity (1.7%), AE not related to Tx (1.7%), and decision (1.7% each). EV dose reductions and interruptions occurred in 25% and 50% of pts. P was interrupted in 6.7%. Grade 3-4 toxicities in 14 pts (23.3%); most common were asthenia (6.7%), rash, bullous dermatitis, diarrhea and vomiting (3.3% each).

Conclusions

EV+P was safe, achieving a promising BOR in advanced melanoma in this preliminary analysis. Correlative analyses, including NECTIN-4, are ongoing.

Clinical trial identification

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Legal entity responsible for the study

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Disclosure

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