TPS9594 **Poster Session**

A multicenter, randomized, controlled, open-label, phase 2 study of the PD-1/IL-2$^{\alpha\text{-bias}}$ bispecific antibody fusion protein IBI363 in mucosal and acral melanoma.

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Background: Although several immune checkpoint inhibitors have been approved for advanced melanoma, there remain significant unmet clinical needs, particularly for immune-cold subtypes such as mucosal and acral melanoma, which are frequently observed in Chinese patients (pts). IBI363 targets and activates tumor-specific T cells that express both PD-1 and IL-2Rα, leading to enhanced antitumor activity and reduced toxicity. Previous phase 1 studies of IBI363 reported manageable safety profiles with encouraging efficacy in advanced melanoma (2024 ASCO Annual Meeting [9562], ESMO Virtual Plenary [VP4-2024], SITC [1502]). Here, we present the trial in progress of a phase 2 study evaluating efficacy and safety of IBI363 monotherapy versus pembrolizumab in mucosal and acral melanoma. **Methods:** This multicenter, randomized, controlled, open-label, phase 2 study planned to enroll 180 pts. Main inclusion criteria are: 1) locally advanced unresectable or metastatic mucosal or acral melanoma; 2) no previous systemic treatment for melanoma; 3) at least one measurable tumor lesion (target lesions) per RECIST v1.1. Pts with active or symptomatic central nervous system metastasis are excluded. Pts are randomized in a 1:1 ratio to receive IBI363 1 mg/kg Q2W (with a priming dose of 100 μg/kg administered 7 days before the full dose) in the experimental arm or to receive pembrolizumab 200 mg Q3W in the control arm. Stratification factors include subtype (mucosal vs acral) and M staging (M0 vs M1a(0)/M1b(0) vs M1a(1)/M1b(1) or M1c/M1d, (0) indicating baseline lactate dehydrogenase [LDH] $\leq$ upper limit normal [ULN] and (1) indicating baseline LDH $>$ ULN). The primary endpoint is progression-free survival (PFS) assessed by independent radiological review committee (IRRC) per RECIST v1.1. The secondary endpoints include investigator-assessed PFS, IRRC-assessed and investigator-assessed objective response rate (ORR), disease control rate (DCR), duration of response (DoR), time to response (TTR) per RECIST v1.1, overall survival (OS), safety, pharmacokinetics (PK) and immunogenicity. No interim analysis is planned. A total of 118 PFS events among 180 pts is estimated to demonstrate the superior efficacy of IBI363 compared to the control, with a power of 90% (α=0.025, one-sided). Clinical trial information: CTR20250280. Research Sponsor: Innovent Biologics (Suzhou) Co., Ltd.