TPS9595 **Poster Session**

NivoReach: Integrated study to demonstrate similarity of JPB898 to reference nivolumab in combination with ipilimumab in patients with advanced melanoma.

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Background: JPB898 is being developed as a biosimilar to reference nivolumab. Analytical and functional in vitro similarity of JPB898 to reference nivolumab has been demonstrated. NivoReach will assess the pharmacokinetic (PK) and efficacy similarity of JPB898 to reference nivolumab in patients with untreated advanced melanoma. Induction therapy with nivolumab 1 mg/kg and ipilimumab 3 mg/kg is approved for advanced melanoma, before nivolumab maintenance therapy. However, the unfavorable toxicity profile of this regimen, attributed mainly to ipilimumab, has led to investigation of alternative regimens. The Phase IIIb/IV CheckMate 511 trial compared the approved regimen with an "inverse dosing" regimen comprising nivolumab 3 mg/kg and ipilimumab 1 mg/kg. Similar response and overall survival rates were observed between the treatment groups, as well as a lower incidence of immune-related toxicities and a lower rate of discontinuation due to treatment-related adverse events with the inverse regimen versus the approved regimen (Lebbé C, et al. J Clin Oncol 2019;37: 867–75). Therefore, inverse dosing is an appealing combination regimen for use in NivoReach, providing a treatment option with a more favorable risk–benefit ratio to a broader advanced melanoma patient population versus the approved regimen. Currently, the study is approved in 19 countries, including the USA and some EU member states. **Methods:** This global, randomized, double-blind, parallel-group study is recruiting participants with untreated, unresectable Stage III or metastatic Stage IV melanoma, measurable per RECIST v1.1. Participants must have an ECOG performance status ≤1. Participants will not be eligible if they have active brain metastases, ocular melanoma, or other active malignancy that is untreated or requires concomitant systemic therapy. Eligible participants will be randomized 2:1:1 to JPB898, or US-licensed or EU-authorized nivolumab, in combination with ipilimumab. Randomization will be stratified by *BRAF* V600 mutation status, PD-L1 expression status, and metastasis stage. In the 12-week induction phase, participants will receive 4 cycles of the inverse regimen (nivolumab 3 mg/kg + ipilimumab 1 mg/kg, Q3W). In the maintenance phase, participants will receive fixed-dose monotherapy (480 mg, Q4W) with JPB898 or reference nivolumab from Week 16 to 48. The co-primary PK endpoints are area under the serum concentration–time curve (AUC) after the first dose and AUC after the fourth dose in the induction phase. The primary efficacy endpoint is best overall response (complete or partial response) up to 28 weeks. Other PK, efficacy, safety, and immunogenicity endpoints will also be assessed up to 52 weeks. The planned randomized sample size is 720 participants. Clinical trial information: NCT06587451. Research Sponsor: Sandoz.