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Title: Phase 1b study of tarlatamab, a half-life extended bispecific T-cell engager (HLE BiTE immune therapy) targeting DLL3, in de novo or treatment emergent neuroendocrine prostate cancer (NEPC).[Report]

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Abstract: TPS197

Background: NEPC is an aggressive cancer with no standard treatment approach and poor prognosis. It is usually treatment-emergent, occurring in 15%-20% of patients (pts) with metastatic castration-resistant prostate cancer following treatment with androgen signaling inhibitors (ASI) and is characterized by histological transformation from adenocarcinoma to a high-grade neuroendocrine tumor.1 The tumor associated antigen delta-like ligand 3 (DLL3) has been identified as a promising target in both NEPC and small cell lung cancer (SCLC), as it is highly expressed in these tumors and minimally expressed on normal tissue. Tarlatamab is a DLL3-targeting HLE BiTE(R) immune therapy designed to bind DLL3 on cancer cells and CD3 on T cells, resulting in T cell activation and expansion and T cell-dependent killing of tumor cells. In preclinical studies, tarlatamab induced T-cell dependent lysis of DLL3-expressing neuroendocrine tumor cell lines, including NEPC cells.2 Interim results of an ongoing first-in-human study in pts with SCLC (NCT03319940) show evidence for tarlatamab efficacy with an acceptable safety profile.3 Together, these findings support a clinical study of tarlatamab in NEPC. Methods: NCT04702737 is an open-label, phase 1b study evaluating tarlatamab infusion in pts with metastatic de novo or treatment-emergent NEPC, consisting of dose exploration and then dose expansion. Key eligibility criteria include adults (>=18 y) with metastatic NEPC whose disease progressed/recurred after >=1 prior line of systemic therapy (platinum-based regimen for de novo NEPC or an ASI if treatment-emergent), measurable disease per RECIST 1.1 with Prostate Cancer Working Group 3 modifications, and ECOG performance status <=2. Primary objectives are to evaluate safety and tolerability and determine the maximum tolerated dose or

recommended phase 2 dose of tarlatamab. Secondary objectives are to evaluate antitumor activity (as assessed by objective response, duration of response, progression-free survival, overall survival, and disease control rate) and characterize pharmacokinetics. Four US and international study sites have been activated with two enrolled pts. References: Aggarwal R, et al. J Clin Oncol. 2018;36:2492-2503. Cooke K, et al. Abstract 627. Presented at: SITC Annual Meeting, Nov 9-14, 2020; Virtual. Owonikoko TK, et al. Abstract 8510. Presented at: ASCO Annual Meeting, June 4-8, 2021; Virtual. Clinical trial information: NCT04702737.

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