Avelumab

Avelumab, sold under the brand name Bavencio, is a fully human Monoclonal antibody therapy for Merkel cell carcinoma, urothelial carcinoma, and renal cell carcinoma.

AMPLIFY-NEOVAC is a randomized 3-arm, window-of-opportunity, multicenter national phase 1 trial to assess the safety, tolerability, and immunogenicity of IDH1-vac combined with avelumab (AVE), an immune checkpoint inhibitor (ICI) targeting programmed death-ligand 1 (PD-L1). The target population includes patients with resectable IDH1R132H-mutant recurrent astrocytoma or oligodendroglioma after standard of care (SOC). Neoadjuvant and adjuvant immunotherapy will be administered to 48 evaluable patients. In arm 1, 12 patients will receive IDH1-vac; in arm 2, 12 patients will receive the combination of IDH1-vac and AVE, and in arm 3, 24 patients will receive AVE only. Until disease progression according to immunotherapy response assessment for neuro-oncology (iRANO) criteria, treatment will be administered over a period of a maximum of 43 weeks (primary treatment phase) followed by facultative maintenance treatment.

Perspective: IDH1R132H 20-mer peptide is a shared clonal driver mutation-derived neoepitope in diffuse gliomas. IDH1-vac safely targets IDH1R132H in newly diagnosed astrocytomas. AMPLIFY-NEOVAC aims at (1) demonstrating the safety of enhanced peripheral IDH1-vac-induced T cell responses by combined therapy with AVE compared to IDH1-vac only and (2) investigating intra-glioma abundance and phenotypes of IDH1-vac induced T cells in exploratory post-treatment tissue analyses. In an exploratory analysis, both will be correlated with clinical outcome [1)].

The combination of avelumab plus axitinib has an acceptable toxicity profile but did not meet the prespecified threshold for activity justifying further investigation of this treatment in an unselected population of patients with rGB [2)].

To date, five drugs have been approved for use in patients with encephalic metastases of lung carcinoma: the anti-PD-1 drugs, pembrolizumab and nivolumab, and the anti-PD-L1 agents, atezolizumab, durvalumab, and avelumab. In recent years, clinical trials of inhibitors in combination with other drugs to treat brain metastasis have also emerged. This review summarizes the biological principles of PD-1/PD-L1 immunotherapy for brain metastasis of lung cancer, as well as ongoing clinical trials to explore unmet needs [3)].

Giles et al. found that programmed cell death ligand 1 (PD-L1) was highly expressed in multiple human malignant meningioma cell lines and patient tumor samples. PD-L1 was targeted with the anti-PD-L1 antibody avelumab and directed natural killer cells to mediate antibody-dependent cellular cytotoxicity (ADCC) of PD-L1-expressing meningioma tumors both in vitro and in vivo. ADCC of meningioma cells was significantly increased in target cells that upregulated PD-L1 expression and, conversely, abrogated in tumor cells that were depleted of PD-L1. Additionally, the high-affinity natural killer cell line, haNK, outperformed healthy donor NK cells in meningioma ADCC. Together, these data support a clinical trial designed to target PD-L1 with avelumab and haNK cells, potentially offering a novel immunotherapeutic approach for patients with malignant meningioma [4].

1)
Bunse L, Rupp AK, Poschke I, Bunse T, Lindner K, Wick A, Blobner J, Misch M, Tabatabai G, Glas M, Schnell O, Gempt J, Denk M, Reifenberger G, Bendszus M, Wuchter P, Steinbach JP, Wick W, Platten M. AMPLIFY-NEOVAC: a randomized, 3-arm multicenter phase I trial to assess safety, tolerability and immunogenicity of IDH1-vac combined with an immune checkpoint inhibitor targeting programmed death-ligand 1 in isocitrate dehydrogenase 1 mutant gliomas. Neurol Res Pract. 2022 May 23;4(1):20. doi: 10.1186/s42466-022-00184-x. PMID: 35599302.
2)
Awada G, Ben Salama L, De Cremer J, Schwarze JK, Fischbuch L, Seynaeve L, Du Four S, Vanbinst AM, Michotte A, Everaert H, Rogiers A, Theuns P, Duerinck J, Neyns B. Axitinib plus avelumab in the treatment of recurrent glioblastoma: a stratified, open-label, single-center phase 2 clinical trial (GliAvAx). J Immunother Cancer. 2020 Oct;8(2):e001146. doi: 10.1136/jitc-2020-001146. PMID: 33067319; PMCID: PMC7570224.
3)
Wang S, Hu C, Xie F, Liu Y. Use of Programmed Death Receptor-1 and/or Programmed Death Ligand 1 Inhibitors for the Treatment of Brain Metastasis of Lung Cancer. Onco Targets Ther. 2020 Jan 23;13:667-683. doi: 10.2147/OTT.S235714. PMID: 32158220; PMCID: PMC6986404.
4)
Giles AJ, Hao S, Padget M, Song H, Zhang W, Lynes J, Sanchez V, Liu Y, Jung J, Cao X, Fujii R, Jensen R, Gillespie D, Schlom J, Gilbert MR, Nduom EK, Yang C, Lee JH, Soon-Shiong P, Hodge JW, Park DM. Efficient ADCC killing of meningioma by avelumab and a high-affinity natural killer cell line, haNK. JCI Insight. 2019 Oct 17;4(20):e130688. doi: 10.1172/jci.insight.130688. PMID: 31536478; PMCID: PMC6824312.