Isocitrate dehydrogenase (IDH) mutations are disease-defining mutations in IDH-mutant astrocytomas and Oligodendroglioma IDH-mutant and 1p/19q-codeleted. In more than 80% of these tumors, point mutations in IDH type 1 (IDH1) lead to the expression of the tumor-specific protein IDH1R132H. IDH1R132H harbors a major histocompatibility complex class II (MHCII)-restricted neoantigen that was safely and successfully targeted in a first-in-human clinical phase 1 trial evaluating an IDH1R132H 20-mer peptide vaccine (IDH1-vac) in newly diagnosed astrocytomas concomitant to the standard of care (SOC).

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 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 maximum 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 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)].

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.