Rindopepimut

Rindopepimut is an investigational immunotherapy that targets the tumor specific oncogene EGFRvIII.

Rindopepimut is administered via intradermal injection and consists of the EGFRvIII-specific peptide sequence conjugated to the carrier protein Keyhole Limpet Hemocyanin (KLH).

Rindopepimut stimulates the patient's immune system, inducing pronounced EGFRvIII-specific humoral and cellular responses. 85% of patients in clinical trials evaluating rindopepimut developed significant anti-EGFRvIII antibody titers, which increased with time on study. The majority (67%) of these patients developed titers above 1:12,800. Such immune responses may contribute to the direct destruction of tumor cells expressing EGFRvIII.

Phase 2 trials

Three Phase 2 trials of rindopepimut have been completed in newly diagnosed EGFRvIII-positive glioblastoma patients with consistent results—ACTIVATE, ACT II, ACT III —and multiple patients continue to be followed for survival. Across all three studies, rindopepimut has been generally well tolerated with generation of robust, specific and durable immune responses. The most common adverse events for rindopepimut include injection site reactions, fatigue, rash, nausea and pruritus.

Phase 3 trials

Rindopepimut is currently being studied in two clinical trials—an international Phase 3 study called ACT IV and a Phase 2 study called ReACT. At the Society for Neuro-Oncology Annual Meeting (SNO) in November 2014, the Company reported interim data from the Phase 2 ReACT study of rindopepimut in recurrent glioblastoma. The Phase 3 ACT IV Study of Rindopepimut in Newly Diagnosed Glioblastoma

ACT IV

The ACT IV study is a randomized, double-blind, controlled study of rindopepimut plus GM-CSF added to standard of care temozolomide in patients with newly diagnosed, surgically resected, EGFRvIII-positive glioblastoma. Patients are randomized into a treatment or control arm after the completion of surgery and standard chemoradiation. The treatment arm regimen includes a vaccine priming phase post-radiation, followed by an adjuvant temozolomide and vaccine maintenance therapy phase. Patients are treated until disease progression. The control arm regimen includes standard of care temozolomide plus injections of Keyhole Limpet Hemocyanin (KLH). KLH is a component of rindopepimut and was selected due to its ability to generate an injection site reaction similar to that observed with the rindopepimut vaccine, which improves the blinding of the study. The primary objective of the study is to determine whether rindopepimut plus GM-CSF improves the overall survival of patients with newly diagnosed EGFRvIII-positive glioblastoma after gross total resection (GTR) when compared to treatment with the current standard of care, temozolomide. 745 patients were enrolled at over 200 centers worldwide to recruit 374 patients with GTR to be included in the primary analysis. Secondary endpoints include: progression free survival; safety and tolerability of rindopepimut and GM-CSF in combination with temozolomide; neurologic status and quality of life.

The Phase 2 ReACT Study of Rindopepimut in Recurrent Glioblastoma

ReAct

The ReACT study is a Phase 2 trial of rindopepimut in combination with Avastin® (bevacizumab) in patients with recurrent EGFRvIII-positive glioblastoma. The study enrolled 125 patients in a first or second relapse of glioblastoma following receipt of standard therapy and is being conducted at approximately 20 sites across the United States. Group 1 enrolled 72 bevacizumab naive patients randomized to receive either rindopepimut or a control injection of Keyhole Limpet Hemocyanin (KLH) in a blinded fashion; all patients are also receiving Avastin. Additionally, group 2 includes 25 patients refractory to bevacizumab, having received bevacizumab in either the frontline or recurrent setting with subsequent progression who are receiving rindopepimut plus bevacizumab in a single treatment arm. In August 2013, we reported that an expansion cohort (group 2C) of patients refractory to bevacizumab was added to better characterize the potential activity of rindopepimut in the refractory patient population. 28 patients were enrolled into this group. All patients will be evaluated for the progression rate at six months, objective response rate, overall survival (OS), and progression free survival. In November 2014, the Company reported interim data from the ReACT study. Across both Group 1 and Group 2, rindopepimut plus bevacizumab was very well tolerated and the results demonstrated promising signs of clinical activity in advanced patient populations.

Zussman BM, Engh JA. Outcomes of the ACT III Study: Rindopepimut (CDX-110) Therapy for Glioblastoma. Neurosurgery. 2015 Jun;76(6):N17. doi: 10.1227/01.neu.0000465855.63458.0c. PubMed PMID: 25985004.