IT-28. VACCINATION AGAINST EPIDERMAL GROWTH FACTOR RECEPTOR VARIANT III IN GLOBLASTOMA: THE RINDOPEPIMUT COMPASSIONATE USE EXPERIENCE

Evangelia Razis1, Gordana Vlahovic2, Lawrence Recht3, Helen Wheeler4, David Reardon5, Kelly Nicholas6, Scott Overy7, Elsa Paradise8, Michael Yellin8, Thomas Davis8, Michael Weller9, Roger Stupp9,10, and Andreas F. Hottinger10; 1Hygeia Hospital, Athens, Greece; 2Duke University, Durham, NC, USA; 3Stanford University Medical Center, Palo Alto, CA, USA; 4Sydney Neuro Oncology Group, Sydney, Australia; 5Dana Farber Cancer Institute, Boston, MA, USA; 6Montreal Neurologic Institute, Montreal, Canada; 7University of Chicago, Chicago, IL, USA; 8Celldex Therapeutics, Inc., Hampton, NJ, USA; 9University Hospital Zurich, Zurich, Switzerland; 10Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

The tumor-specific epidermal growth factor receptor variant III mutation (EGFRvIII) is widely expressed in glioblastoma and thus represents an attractive target for immunotherapeutic approaches. The investigational vaccine rindopepimut is an EGFRvIII peptide sequence conjugated to keyhole limpet hemocyanin and is administered intradermally with GM-CSF. Previous single-arm studies of rindopepimut in newly diagnosed, resected, EGFRvIII+ glioblastoma have shown encouraging PFS and OS. This compassionate use program provided rindopepimut to 61 EGFRvIII+ glioblastoma patients who were ineligible for ongoing clinical trials. Data are currently available on 42 patients, 12 (29%) with newly diagnosed glioblastoma (resected or inoperable) and 30 (71%) with recurrent disease. MGMT methylation was seen in 9/17, while all tested patients were negative for IDH1 (12/12) and IDH2 (7/7). Median age was 53 years (15-70) and median time from diagnosis was 14.5 months (2.7-58.7). Rindopepimut, administered in combination with temozolomide (57%), bevacizumab (57%), and/or other (17%), was well tolerated, with frequent mild injection site reactions and one potentially treatment-related, serious event of cerebral edema. Median peak rindopepimut-induced anti-EGFRvIII titer was 1:1,200 (1:100-1:6,553, 600). Median treatment duration is currently 3.7 (0.03-60.1) months. Tumor response (>50% shrinkage in measurable disease) was observed in six patients receiving rindopepimut with other agents. One inoperable glioblastoma patient experienced a CR during treatment with rindopepimut, erlotinib, temozolomide, and bevacizumab, and has continued rindopepimut for >5 years without significant toxicity or disease recurrence. Biopsy at recurrence showed EGFRvIII was eliminated in a patient who received rindopepimut and temozolomide for ~9 months. In patients with newly diagnosed and recurrent glioblastoma, respectively, median PFS was 9.1 and 2.5 months, and median OS was 15.7 and 8.7 months from first vaccination. In conclusion, rindopepimut in combination with various anticancer therapies resulted in robust anti-EGFRvIII humoral response with minimal toxicity. PFS and OS appear promising in this heterogeneous, poor prognosis population.