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Authors
Reardon, DA
Schuster, JM
Tran, DD
et al.

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IMCT-08. ReACT: LONG-TERM SURVIVAL FROM A RANDOMIZED PHASE II STUDY OF RINDOPEPIMUT (CDX-110) PLUS BEVACIZUMAB IN RELAPSED GliOBLASTOMA

David A. Reardon1, Annick Desjardins2, James Schuster3, David D. Tran4, Karen L. Fine5, Louis B. Nabors6, Gordon Li7, Daniela A. Bota8, Rimas V. Lukas9, Lynn S. Ashby10, J. Paul Dui11, Maciej M. Mrugala12, Andrea Werner13, Laura Vitale13, Yi He13, Jennifer Green13, Michael J. Yellin13, Christopher D. Turner13, Thomas A. Davis13, and John H. Sampson2;

1Dana-Farber Cancer Institute, Boston, MA, USA; 2Duke University Medical Center, Durham, NC, USA; 3University of Pennsylvania, Philadelphia, PA, USA; 4Washington University, St. Louis, MO, USA; 5Baylor Research Institute, Dallas, TX, USA; 6University of Alabama at Birmingham, Birmingham, AL, USA; 7Stanford University School of Medicine, Stanford, CA, USA; 8UC Irvine Medical Center, Irvine, CA, USA; 9University of Chicago, Chicago, IL, USA; 10Barrow Neurological Institute, Phoenix, AZ, USA; 11Long Island Brain Tumor Center at Neurological Surgery, P.C., Lake Success, NY, USA; 12University of Washington School of Medicine, Seattle, WA, USA; 13Celldex Therapeutics, Inc., Hampton, NJ, USA

BACKGROUND: EGFRvIII, a constitutively active EGFR deletion driver mutation, is associated with poor long-term survival in glioblastoma (GB). The investigational vaccine rindopepimut consists of an EGFRvIII-specific peptide sequence conjugated to keyhole limpet hemocyanin (KLH), delivered intradermally with GM-CSF. Three phase II studies in newly diagnosed, resected, EGFRvIII+ GB demonstrated encouraging progression-free survival (PFS), overall survival (OS) and safety. METHODS: In the Phase II “ReACT” study, 73 bevacizumab (BV)-naïve pts in 1st or 2nd relapse with EGFRvIII+ GB were randomized 1:1 to BV plus double-blinded injection of rindopepimut or control (KLH). Endpoints: 6-month PFS (PFS6; primary; target α = 0.2 by 1-sided chi-square test), objective response rate (ORR), PFS, OS and safety. RESULTS: Primary rindopepimut toxicity is Grade 1-2 injection site reaction. For rindopepimut + BV vs. KLH + BV (per centralized review; RANO criteria): PFS6 = 28% (10/36) vs. 16% (6/37) (p = 0.116); ORR = 30% (9/30) vs. 18% (6/34). Cessation of steroids 2 months: 44% (8/18) vs 21% (4/19), >6 months: 33% (6/18) vs. 0. Median (95% CI) OS = 11.6 (10.0, 16.2) vs. 9.3 (7.1, 11.3) months (HR = 0.57 [0.33, 0.98], p = 0.039). 9 vs 6 pts remain in follow-up; 6 vs. 2 are progression-free. OS analyses adjusted for various prognostic factors consistently favor rindopepimut. Rindopepimut induced robust anti-EGFRvIII titers (1:12,800-1:6,553,600) in 80% of pts. Antibodies, predominantly IgG1 isotype, mediate killing of EGFRvIII+ tumor cells through ADCC and CDCC in vitro. Within the rindopepimut arm, peak titer (≥ 1:12,800 at any time) and rapid titer generation (≥ 1:12,800 by Day 57) were associated with prolonged OS (HR = 0.16, p = <0.0001 and HR = 0.59, p = 0.182, respectively). Evaluation of humoral response quality, HLA typing vs. outcome, and survival follow-up continue. In an additional cohort of BV-exposed pts (n = 53), four pts experienced objective tumor response. CONCLUSIONS: Rindopepimut induces potent EGFRvIII-specific immune response and tumor regression, and appears to significantly prolong survival when administered with BV, in pts with relapsed GB.