UC Irvine

UC Irvine Previously Published Works

Title

107 ReACT: Overall Survival From a Randomized Phase II Study of Rindopepimut (CDX-110) Plus Bevacizumab in Relapsed Glioblastoma.

Permalink

<https://escholarship.org/uc/item/3jc65466>

Journal

Neurosurgery, 62 Suppl 1(Supplement 1)

ISSN

0148-396X

Authors

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

Publication Date

2015-08-01

DOI

10.1227/01.neu.0000467069.86811.3f

Peer reviewed

Abstracts

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. Fink⁵, Louis B. Nabors⁶, Gordon Li⁷, Daniela A. Bota⁸, Rimas V. Lukas⁹, Lynn S. Ashby¹⁰, J. Paul Duic¹¹, 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 $\alpha = 0.2$ 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 CDC in vitro. Within the rindopepimut arm, peak titer ($\geq 1:12,800$ at any time) and rapid titer generation ($\geq 1:12,800$ 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.