Title

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Abstracts

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

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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 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.