Title
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ReACT: Overall survival from a randomized phase II study of rindopepimut (CDX-110) plus bevacizumab in relapsed glioblastoma. First Author: David A. Reardon, Dana-Farber Cancer Institute, Boston, MA

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 a peptide sequence unique to EGFRvIII conjugated to keyhole limpet hemocyanin (KLH), delivered intradermally with GM-CSF. Three phase II studies of rindopepimut in newly diagnosed, resected, EGFRvIII+ GB demonstrated encouraging progression-free survival (PFS), overall survival (OS) and safety profile. Compassionate use experience suggests that rindopepimut may also provide benefit in relapsed GB, particularly with agents such as bevacizumab (BV).

Methods: In the Phase II "ReACT" study, 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), objective response rate (ORR), PFS, OS and safety.

Results: Accrual is complete (n = 72); study follow-up continues (n = 30). Primary rindopepimut toxicity is Grade 1-2 injection site reaction. For rindopepimut + BV vs. KLH + BV (per investigator; RANO criteria): PFS6 = 27% (9/33) vs. 11% (4/35) (p = 0.048, 1-side chi-square test); ORR = 24% (7/29) vs. 17% (5/30). Central PFS/ORR assessment is underway. Median (95% CI) OS = 12.0 (9.7, -) vs. 8.8 (6.8, 11.4) months (HR = 0.47 [0.25, 0.91]; p = 0.0208), with 8 vs 4 pts progression-free on study. OS analyses favor rindopepimut including when adjusted for various prognostic factors. Rindopepimut induced robust anti-EGFRvIII titers (1:12,800 to 1:6,553,600) in 80% of pts. Rapid anti-EGFRvIII titer generation was associated with prolonged OS (HR = 0.47 [0.18, 1.27]; p = 0.128) within the rindopepimut arm, and was most frequent in pts with KPS ≥ 90 (odds ratio = 9.75; p = 0.007). Additional evaluation of humoral response quality and HLA typing vs. outcome are underway. In an additional cohort of BV-exposed pts (n = 53), four pts experienced objective tumor response.

Conclusions: These near-final data show that 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. Clinical trial information: NCT01498328.