**Identifying the correct patient (pt) population for ABT-414: Biomarker assays for epidermal growth factor receptor (EGFR) in pts with glioblastoma (GBM)**


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**Aim/Background:** Aberrant EGFR signaling plays a vital role in GBM oncogenesis. ABT-414 comprises an EGFR-targeted antibody conjugated to the toxic agent monomethylauristatin F. An open-label, 3-arm, phase I study (NCT01800695) is underway to evaluate 3 different ABT-414 regimens in GBM. To understand the population most suited for ABT-414 therapy, assays measuring EGFR gene amplification/protein overexpression, and the presence of EGFRvIII mutation have been developed.

**Methods:** Total EGFR and EGFRvIII expression were measured with reverse transcription-polymerase chain reaction (RT-PCR). EGFR gene amplification was detected with fluorescence in situ hybridization (FISH) using 2 probes: Vysis locus-specific identifier EGFR probe and Vysis chromosome enumeration probe (CEP) 7 probe. FISH utilized Ratio of EGFR to CEP 7 to identify locus-specific EGFR gene amplification. Total EGFR protein expression was analyzed via immunohistochemical (IHC) using Dako pharmDx™ IHC assay. Relative expression of total EGFR and presence of EGFRvIII mRNA were determined with quantitative RT-PCR. Tumor tissues from 89 pts were used for these tests.

**Results:** IHC and RT-PCR confirmed expression of EGFR mRNA and protein are correlated in GBM tissue samples (Spearman correlation is –0.86, P = 0.0026). A strong association between EGFR gene amplification and mRNA overexpression was observed. EGFRvIII mRNA was detected almost exclusively in cases with EGFR amplification. Thus far, EGFR amplification has been confirmed in 23/29 pts tested. All 6/6 pts with confirmed objective radiographic responses by Response Assessment in Neuro-Oncology criteria displayed EGFR gene amplification, whereas only 5/6 pts had total EGFR mRNA overexpression using RT-PCR. EGFRvIII expression by RT-PCR was detected in 4/6 pts.

**Conclusions:** Assays were developed to characterize EGFR gene amplification, EGFR mRNA and protein expression, EGFRvIII status, and used to characterize EGFR status of GBM samples from pts treated with ABT-414 in ongoing phase I trial. When comparing EGFR status to pt outcome, EGFR amplification by FISH had strongest association with objective radiographic responses.

**Clinical trial identification:** NCT01800695

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