ET-19. A PHASE 1 STUDY EVALUATING ABT-414 WITH TEMOZOLOMIDE (TMZ) OR CONCURRENT RADIOTHERAPY (RT) AND TMZ IN GLIOBLASTOMA (GBM)
Hui K. Gan1, Lisa Fichtel2, Andrew B. Lassman3, Ryan Merrell4, Martin van den Bent5, Priya Kumthekar6, Andrew M. Scott1, Michelle Pedersen7, Erica Gomez2, JuDee Fischer2, William Ames7, Hao Xiong7, Matt Dudley7, Wijith Munasinghe7, Lisa Roberts-Rapp7, Peter Ansell7, Kyle Holen7, and David A. Reardon8; 1Austin Health and Ludwig Institute for Cancer Research, Heidelberg VIC, Australia; 2South Texas Oncology and Hematology, San Antonio, TX, USA; 3Columbia University Medical Center and Herbert Irving Comprehensive Cancer Center, New York, NY, USA; 4Northshore University Health System Comprehensive Cancer Center, Evanston, IL, USA; 5Erasmus MC Cancer Center, Rotterdam, The Netherlands; 6Northwestern University, Chicago, IL, USA; 7AbbVie Inc., North Chicago, IL, USA; 8Dana-Farber Cancer Institute, Boston, MA, USA

BACKGROUND: Standard therapies have little effect on the poor survival rates of GBM. Abnormal epidermal growth factor receptor (EGFR) expression and signaling are common in GBM. ABT-414 is a unique antibody-drug conjugate, with a toxic payload (MMAF) targeted to active EGFR or mutant EGFRvIII, that has demonstrated high antitumor activity in preclinical GBM tumor models. METHODS: Objectives were to evaluate the safety, pharmacokinetics (PK), and the maximum tolerated dose (MTD) of ABT-414 when administered with TMZ (recurrent or unresectable GBM, Arm B) or concurrent RT and TMZ (newly diagnosed GBM, Arm A). Adverse events (AEs), PK parameters, objective response (RANO), and tumor tissue EGFR biomarkers were assessed. Dose escalation was determined by the continual reassessment method (CRM). RESULTS: As of April, 2014, 22/21 pts were treated in Arm A/B. Common treatment-emergent AEs included fatigue (n=11/6, Arm A/B); blurred vision (n=10/9); AST increase (n=9, Arm A); and nausea (n=7/7) Grade 3/4 AEs (≥2 pts) included lymphopenia (n=3); eye toxicity (n=3); brain edema, ALT, AST (n=2 each) in Arm A and keratitis (n=2) in Arm B. Doses from 0.5-3.2mg/kg have been explored. Dose limiting toxicities primarily affecting the eye (keratitis) and liveroccurred at multiple doses. The CRM has predicted 2.4mg/kg as the MTD in Arm A and 1.25mg/kg in Arm B. Patient samples are being evaluated for EGFR expression, amplification and EGFRvIII status. Efficacy endpoints are not yet mature in Arm A, but 4 patients in Arm B have best responses of 3 PRs and 1 CR. CONCLUSIONS: PK and safety data support doses of 2.4 and 1.25mg/kg as the predicted MTD in Arms A and B. Preliminary safety data demonstrate liver and eye toxicities in Arm A and primarily eye toxicities in Arm B. Updated biomarker results as they correlate with efficacy will be reported. Phase 2 studies assessing ABT-414 in GBM are planned.