Center, New York, NY, USA, [3]AbbVie Inc., North Chicago, IL, USA, [4]NorthShore University Health System, Glenview, IL, USA

BACKGROUND: Depatuxizumab mafodotin (depatux-m, formerly ABT-414), is an antibody-drug conjugate comprised of an EGFR-targeted antibody, a non-cleavable linker maleimidocaproyl, and the microtubule inhibitor monomethylauristatin F. Promising antitumor activity of depatux-m was observed in patients with glioblastoma (GBM) in Phase 12 studies. Dosage of depatux-m is limited by ocular side effects (OSE), such as blurred vision, dry eye, and photophobia from corneal epitheliopathy, which are generally reversible after dose reduction or drug discontinuation. This Phase 3b study evaluates depatux-m-related OSE management strategies used in depatux-m clinical trials. METHODS: This open-label study will enroll approximately 90 patients with newly diagnosed, histologically confirmed, grade IV GBM that is epidermal growth factor receptor (EGFR)-amplified. Patients will receive depatux-m during the chemoradiation phase (radiation and temozolomide [TMZ]), and during adjuvant therapy with TMZ. Patients are randomized to one of three prophylactic ocular treatments: standard steroids (SS), SS with vasoconstrictors and cold compress (VC), or enhanced steroids (ES) with VC. Primary objective is to evaluate these prophylactic strategies for their effect on the proportion of patients requiring a change in OSE management due to inadequate control of OSEs, defined as either a 3-line decline in visual acuity from baseline or Grade 3 OSE severity on the Corneal Epithelial Adverse Event (CEAE) activities of daily living-based scale. Inadequate control with initial prophylactic regimen will trigger a switch to the addition of bandage contact lenses (BCL). Secondary objective assesses change in OSE management due to inadequate control of OSEs by BCL, defined as percentage of patients with Grade 3 CEAE that will trigger transition of patient to investigator discretion regimen (depatux-m interruption/dose reduction, VC prophylaxis, or ES prophylaxis). ClinicalTrials.gov: NCT03419403.

### ACTR-22. A PHASE I STUDY OF CYTOSINE DEAMINASE-EXPRESSING NEURAL STEM CELLS (CD-NSCs) ADMINISTERED INTRACRANIALLY AND IN COMBINATION WITH ORAL 5-FLUOROCYTOSINE (5-FC) AND LEUCOVORIN IN PATIENTS WITH RECURRENT HIGH GRADE GLIOMA

Jana Portnow[1], Timothy Synold[1], Behnam Badie[2], Suzette Blanchard[2], Julie Kilpatrick[1], Revathiswari Tirughana[1], Marianne Metz[1], Vivi Tran[1] and Karen Aboody[3]; [1]City of Hope, Duarte, CA, USA, [2]City of Hope Beckman Research Institute and Medical Center, Duarte, CA, USA, [3]City of Hope Beckman Research Institute and National Medical Center, Duarte, CA, USA

BACKGROUND: Human NSCs are tumor tropic, making them attractive vehicles for delivery of therapeutics. An immortalized, clonal NSC line was retrovirally transduced to express CD, which converts 5-FC to 5-fluorouracil (5-FU). The primary objectives of this study were to assess the feasibility of serially administering CD-NSCs intracranially via a Rickham catheter and determine the recommended doses for phase II testing (RP2D). METHODS: Adult patients with recurrent high grade gliomas underwent tumor resection or biopsy and placement of a Rickham. CD-NSCs were injected during surgery and thereafter infused through the Rickham every 2 weeks. Three days after each dose of CD-NSCs, patients took 5-FC (and leucovorin—dose level 3 patients only) orally every 6 hours for 7 days. The dose of CD-NSCs was escalated from 50 x $10^6$ to 150 x $10^6$ using a standard 3 + 3 design. 5-FC and leucovorin doses were 37.5 mg/kg and 25 mg, respectively. A treatment cycle was 28 days, with CD-NSCs administered on days 1 and 15, followed by 5-FC (and leucovorin) on days 4–10 and 18–24. Blood samples were drawn to assess for possible anti-NSC antibody and T cell responses. RESULTS: Fifteen evaluable patients received a median of 2 (range 1–5) cycles of study treatment. One dose-limiting toxicity occurred: grade 3 wound infection. Three patients developed anti-NSC antibodies after receiving 3 doses of NSCs. There was no correlation between these results and use of dexamethasone or number of cycles. Analyses of PK and possible anti-NSC T cell responses are ongoing. Three patients had stable disease for 5 months. CONCLUSIONS: Use of a Rickham to serially administer CD-NSCs intracranially is safe and feasible. Study treatment was well tolerated. There were no clinical signs of immunogenicity to these allogeneic CD-NSCs. The RP2D is 150 million CD-NSCs, 37.5 mg/kg of 5-FC, and 25 mg of leucovorin per dose.

### ACTR-23. SAFETY OF INTRA-ARTERIAL CHEMOTHERAPY WITH OSMOTIC OPENING OF THE BLOOD-BRAIN BARRIER

Ryan Priest[1], Prakash Ambady[1] and Edward Neweult[2]; [1]Oregon Health & Science University, Portland, OR, USA, [2]Oregon Health and Science University, Portland, OR, USA

Intra-arterial (IA) infusion of hypertonic mannitol transiently opens the blood-brain barrier (BBB) to improve drug delivery to intracerebral tumors. The aim of this study was to evaluate the safety of osmotic BBB disruption (BBBD) followed by administration of IA chemotherapy. We performed a retrospective chart review of all malignant brain tumor patients who underwent BBBD on six IRB approved treatment protocols or off protocol at Oregon Health and Science University between 1997 and 2017. Toxicities and adverse events (AEs), including death within 30 days of treatment, were assessed. A total of 4018 BBBD procedures were performed on 268 patients (mean 15 BBBD procedures per patient). The most common pathologies were primary central nervous system lymphoma (32%) and anaplastic oligodendroglioma (12%). Most AEs were chemotherapy-related. Only 5% of AEs were attributable to the BBBD procedure, and only 0.42% of these were associated with permanent neurological damage (Grade 3 or 4 SAE). Four SAEs were due to ischemia as detected on magnetic resonance imaging and had minimal impact on quality of life. Four SAEs were due to anterior cord syndrome subsequent to iatrogenic laminar flow of the chemotherapy and were partially responsive to steroids. Subsequently this toxicity was eliminated by procedures to avoid laminar flow. Focal seizures, largely responsive to medical intervention, occurred within 24 hours after 257 (6.4%) BBBD procedures. Most seizures (229, 89%) followed IA administration of methotrexate and were transient and without sequelae. Five patient deaths occurred within 30 days; 1 due to a brain stem stroke related to BBBD, 1 due to a pulmonary embolus, and 3 due to disease progression. We conclude that although the BBBD procedure is invasive, permanent toxicities or death are rare. These results show that osmotic BBBD can be performed safely in brain tumor patients.

### ACTR-25. UPDATED RESULTS FROM A PROSPECTIVE, RANDOMIZED PHASE 2 STUDY IN PATIENTS WITH FIRST RELAPSE OF HIGH-GRADE ASTROCYTOMA USING TVB-2640 IN COMBINATION WITH AVASTIN VERSUS AVASTIN ALONE

Brandon Konkel[1], Laura Caflisch[2], Aldolfo Enrique Diaz Duque[1] and Andrew J. Brenner[1]; [1]Mays Cancer Center/UT Health San Antonio, San Antonio, TX, USA, [2]UT Health San Antonio, San Antonio, TX, USA

BACKGROUND: Standard of care for glioblastoma multiforme (GBM) is surgical resection followed by temozolamide, with Avastin given at relapse. Responses to Avastin remain brief; resistance may involve overexpression of Fatty Acid Synthase (FASN). Our institution is conducting a phase 2 study of Avastin with or without the FASN inhibitor TVB-2640 in patients with GBM in first relapse. METHODS: This is a prospective, randomized, phase 2 study of Avastin with or without TVB-2640 in patients with GBM in first relapse. Primary end point is progression free survival (PFS). Inclusion criteria are: age 18, ECOG 0 to 2, GBM progression following standard combined modality treatment. Randomization is into 2 separate arms. Patients in arm 1 receive Avastin every 2 weeks in combination with TVB-2640. Patients in arm 2 receive Avastin alone every 2 weeks. MR-Spectroscopy (MRS) and serum sampling for exosome analysis will be obtained on all patients at day 1 and 28 of first cycle. Starting on cycle 2 day 1, all patients will converge to a single arm and will continue to receive Avastin in combination with TVB-2640. A total sample size of 24 patients will provide 90% power to detect a 4 month difference in PFS (3 months for Bev alone (historic controls) versus 7 months for TVB-2640 in combination with Bev, (i.e., a hazard ratio of 0.43) using a one-sided log-rank test with alpha=0.1. RESULTS: We have enrolled 13 patients to date, 12 have started therapy; 1 came off study early due to intracranial hemorrhage. No grade 3 or higher treatment related AEs have occurred. Updated results will include PFS, response, and biomarker analysis (exosome, MRS). CONCLUSIONS: The combination of TVB2640 with Avastin appears to be well tolerated. Enrollment will continue with planned completion in early 2019. (Clinical trial registry number: NCT03032484).

### ACTR-26. A FEASIBILITY STUDY OF THE NATIVIS VOYAGER® SYSTEM IN PATIENTS WITH NEWLY DIAGNOSED GLIOBLASTOMA (GBM)

Garni Barkhoudarian[1], Sajeel Chowdhary[2], Nicholas Blondin[3] and Santosh Kesari[4]; [1]John Wayne Cancer Institute, Santa Monica, CA, USA, [2]Marcus Neuroscience Institute, Boca Raton, FL, USA, [3]St. Vincent's Medical Center, Bridgeport, CT, Fairfield, CT, USA, [4]Curtana Pharmaceuticals, Santa Monica, CA, USA

BACKGROUND: The Nativis Voyager® system is a non-sterile, non-invasive, non-thermal, portable, investigational medical device that uses a specific, localized ultra-low radio frequency energy (ulRFE®) cognate for the treatment of brain cancer. METHODS: In this prospective, open-label, multi-center trial, adults newly diagnosed with GBM, following maximal tumor debulking, are eligible for enrollment. The objective of the study is to assess if the Voyager ulRFE therapy is a safe and feasible treatment for newly diagnosed GBM when combined with standard of care (i.e., focal radiotherapy + temozolomide). Patients receive continual therapy with the Voyager, concurrently with radiotherapy + temozolo-