radiographic evidence of new or progressive central nervous system (CNS) metastases after radiation therapy with ≥1 lesion of ≥1 cm in the longest dimension on gadolinium-enhanced magnetic resonance imaging. Patients received nal-IRI 50 mg/m^2 (free-base equivalent; FBE) every two weeks (q2w) as an intravenous infusion over 90 minutes, escalating to 70 mg/m^2 FBE q2w, if tolerated. RECIST v1.1 and modified RECIST criteria were used to assses non-CNS and CNS disease, respectively. RESULTS: In total, 30 patients were enrolled (10 with active BM). Median age was 53 years (range 29–70 years) and median number of prior cytotoxic anti-cancer regimens was 3 (range 0–6); 29 patients received ≥1 dose of nal-IRI 50 mg/m^2 FBE. Overall, nal-IRI monotherapy appeared to be well tolerated, and achieved ≥30% objective response rates for both CNS and non-CNS disease. Among the 10 patients with active BM, 6 achieved CNS disease control (3 partial responses [PRs] and 3 stable disease [SD]), including one patient with durable CNS SD and non-CNS PR for 2 years. Among 7 patients with serial evaluation of CNS metastases posttreatment, 6 patients achieved a reduction in target CNS lesions compared with baseline. CONCLUSION: Treatment with nal-IRI resulted in CNS disease control among 6 of 10 heavily pretreated patients with mBC and active BM. Further exploration of nal-IRI in patients with mBC and active BM is warranted.

TRLS-07. BRAINSTORM: OUTCOMES FROM A MULTI-INSTITUTIONAL PHASE I/II STUDY OF RRX-001 IN COMBINATION WITH WHOLE BRAIN RADIATION THERAPY FOR PATIENTS WITH BRAIN METASTASES

Michelle Kim[1], Hemant Parmar[1], Matthew Schipper[1], Theresa Devasia[1], Madhava Aryal[1], Santosh Kesari[2], Steven O'Day[2], Aki Morikawa[1], Daniel Spratt[1], Larry Junck[1], Aaron Mammoser[3], James Hayman[1], Theodore Lawrence[1], Christina Tsien[4], Robert Aiken[5], Sharad Goyal[6], Nacer Abrouk[7], Malcolm Trimble[8], Yue Cao[1], and Christopher Lao[1]; [1]University of Michigan, Ann Arbor, MI, USA, [2]John Wayne Cancer Institute, Santa Monica, CA, USA, [3]Louisiana State University Health Science Center, New Orleans, LA, USA, [4]Washington University, St. Louis, MO, USA, [5]Rutgers Cancer Institute, New Brunswick, NJ, USA, [6]George Washington University, Washington, DC, USA, [7]Clinical Trials Innovations, Mountain View, CA, USA, [8]Henry Ford Allegiance Health, Detroit, MI, USA

INTRODUCTION: To determine the recommended Phase II dose of RRx-001, a radiosensitizer with vascular normalizing properties, when used with whole-brain radiation therapy (WBRT) for brain metastases, and to assess whether quantitative changes in perfusion MRI after RRx-001 correlate with response. METHODS AND MATERIALS: Five centers participated in this phase I/II trial of RRx-001 given once pre-WBRT then twice weekly during WBRT (30 Gy/10 fractions). Four dose levels were planned (5 mg/m2, 8.4 mg/m2, 16.5 mg/m2, 27.5 mg/m2). Dose-escalation was managed by the Time-to-Event Continual Reassessment Model (TITE-CRM). Correlative DCE-MRI was performed in a subset of patients and linear mixed models used to correlate change in 24-hour T1, Ktrans (capillary permeability) and Vp (plasma volume) with change in tumor volume. RESULTS: Between 2015–2017, 31 patients were enrolled. Two patients dropped out prior to any therapy and 7 were treated with concurrent temozolomide following a study amendment. Median age was 60 years (range, 30–76) and 17 were male. The most common tumor types were melanoma (58%) and non-small cell lung cancer (20%). No dose-limiting toxicities were observed. The most common severe adverse event was grade 3 asthenia in 6.9% (2/29). The median intracranial response rate was 46% (95%CI 24–68) and median overall survival was 5.2 months (95%CI 4.5–9.4). No neurologic deaths occurred. Among 10 evaluable patients undergoing DCE-MRI, a reduction in Vp 24 hours after RRx-001 was associated with reduced tumor volume at 1 month and 4 months (p≤0.01). CONCLUSION: The addition of RRx-001 to WBRT is safe and well-tolerated with favorable intracranial response rates. Because activity was observed across all dose levels, and in the absence of a dose response, the recommended Phase 2 dose is 10 mg administered twice weekly. A reduction in Vp by DCE-MRI 24 hours after RRx-001 suggests anti-angiogenic activity that is associated with longer-term tumor response.

TRLS-08. CNS PENETRATION AND PRELIMINARY EFFICACY OF SACUTIZUMAB GOVITECAN IN BREAST BRAIN METASTASIS AND GLIOBLASTOMA: A SURGICAL STUDY

Andrew Brenner, John Floyd, Prathiba Surapaneni, Vinu Madhusudanan-Kunnuparampil, and Stefano Tiziani; UT Health Science Center, San Antonio, TX

Sacituzumab govitecan (SG) is an antibody drug conjugate (ADC) that targets Trop-2 for the selective delivery of SN-38 to tumors. SG carries SN-38, a topoisomerase inhibitor active in the nanomolar range for most cells (including TNBC and GBM) and freely cross the blood brain barrier. SN-38 is conjugated to SG by a linker designated CL2A which is sensitive to acidic conditions. SG has since been granted priority review designation by the FDA, with approval anticipated for triple negative breast cancer. Brain metastases is a significant concern in this patient population, but whether this agent is able to target the CNS through the blood brain barrier is unknown. Based upon the characteristics of this specific ADC, including the use of a pH labile linker and a payload with good CNS penetration, it is our specific hypothesis that the SG can achieve intratumoral concentrations of SN-38 sufficient to achieve therapeutic benefit in patients with neoplastic involvement of the brain. We further hypothesize that while total concentration of SN-38 will correlate with expression of trop2, free SN-38 will correlate more strongly with intratumoral hypoxia. To address this, we are performing a non-randomized, prospective study of SG in subjects with CNS involvement and planned surgical resection. SG is given as single dose at 10mg/kg pre-operatively on Day-1. Surgery will be followed by post-operative treatment with sacituzumab govitecan given intravenously with standard dose of 10 mg/kg on day1 and day 8 of 21-day cycle, until disease progression. Approximately 20 patients, 2 cohorts of 10 patients each with GBM and breast brain tumors, will be enrolled. Tumors will be analyzed for total antibody, free SN-38, and total SN-38 (free SN-38 + Antibody-SN38) concentrations in tumor tissue. Correlations will be made to Trop2 expression and hypoxia. Interim results will be presented.

TRLS-09. RTOG1119: PHASE II RANDOMIZED STUDY OF WHOLE BRAIN RADIOTHERAPY / STEREOTACTIC RADIOSURGERY IN COMBINATION WITH CONCURRENT LAPATINIB IN PATIENTS WITH BRAIN METASTASIS FROM HER2-POSITIVE BREAST CANCER

In Ah Kim[1], Kathryn Winter[2], David Peereboom[3], Paul Sperduto[4], Jennifer De Los Santos[5], Tomi Ogunleye[6], Daniel Boulter[7], Julia White[7], and Minesh Mehta[8]; [1]Seoul National University, Seoul, Republic of Korea, [2]NRG Oncology Statistics and Data Management Center, Philadelphia, PA, USA, [3]Cleveland Clinic Main Campus, Cleveland, OH, USA, [4]Ridgeview Regional Radiation Oncology, Saint Louis Park, MN, USA, [5]Grandview Medical Center, Birmingham, AL, USA, [6]Northside Hospital Cancer Institute, Atlanta, GA, USA, [7]The Ohio State University Wexner Medical Center, Columbus, OH, USA, [8]Miami Cancer Institute, Miami, FL, USA

The addition of trastuzumab to cytotoxic chemotherapy has improved outcomes for patients with HER2 positive breast cancer. Increased survival coupled with limited blood-brain barrier (BBB) penetration of trastuzumab may contribute to the increased incidence of brain metastasis in these patients. Half of these patients die of intracranial disease progression rather than extracranial disease. Therefore, strategies to improve survival must include increased CNS disease control in these patients. Lapatinib crosses the BBB and demonstrates modest activity against intracranial metastases. Based upon preclinical data and results of a phase I study, we hypothesized that lapatinib plus WBRT /SRS can improve the intracranial disease control compared to WBRT / SRS alone. A randomized phase II trial of WBRT (37.5 Gy/3 weeks) or SRS plus or minus concurrent lapatinib (daily 1000 mg for 6 weeks) was initiated. CNS penetrating HER2 targeted therapy is permitted throughout the study, but patients not on trastuzumab, pertuzumab or any other breast cancer therapy at study entry are not permitted to begin this therapy while on protocol treatment, but may begin it 24 hours after completion of protocol treatment. Eligibility includes HER2+ breast cancer with at least one measurable, unirradiated parenchymal brain metastasis. The two populations targeted for accrual include patients with 1) newly diagnosed, multiple brain metastases or 2) progressive brain metastases after stereotactic radiosurgery (SRS) or surgical resection of 1–3 metastases. Prior lapatinib is allowed. Patients are stratified by breast-specific graded prognostic assessment; use of non-CNS penetrating HER2 targeted therapy; and prior SRS or surgical resection. The primary endpoint is complete response rate in the brain 12 weeks after WBRT. Secondary endpoints include objective response rate, lesion-specific response rate, CNS progression-free survival, and overall survival. 140 of 143 target accrual have enrolled (4/22/2019).

TRLS-10. MITIGATING NEUROCOGNITIVE DEFICITS FROM WHOLE-BRAIN RADIOTHERAPY IN PATIENTS WITH NUMEROUS BRAIN METASTASES VIA A NOVEL SUPEROXIDE DISMUTASE MIMETIC: RATIONALE & DESIGN OF A CLINICAL TRIAL

John Kirkpatrick[1], Heather Franklin[1], Jordan Torok[1], Scott Floyd[1], Carey Anders[1], Peter Fecci[1], April Salama[1], Jeffrey Clarke[1], Daniel George[1], James Crapo[2], and Katherine Peters[1]; [1]Duke University Medical Center, Durham, NC, USA, [2]BioMimetix Pharmaceutical, Inc., Greenwood Village, CO, USA

BACKGROUND: Patients with a large number of brain metastases (BM) and/or micrometastatic disease in the brain present a clinical challenge. While technical innovations in stereotactic radiosurgery (SRS) have extended the number of BM that can be effectively treated, SRS does not treat occult disease and distant brain failure (DBF) post-SRS remains high. Immuno- and targeted therapies show promise in treating metastatic disease to the brain, though response rates are variable. In contrast, whole-brain radiotherapy (WBRT) provides high rates of local control and, compared