lymphodepletion followed by 3-doses of IV CYNK-001 weekly. In the IT cohort, subjects undergo placement of an IT catheter with an ommaya reservoir followed by 3-doses of IT CYNK-001 weekly. Patients are monitored for 28-days after last infusion for toxicity. Once maximum safe dose (MSD) is determined, patients undergo IV or IT treatments at MSD followed by surgical resection and the tumor tissue will be analyzed for NK cell engraftment and persistence. We will utilize a 3 + 3 dose de-escalation design (maximum n=36). Primary endpoint is safety and feasibility. Secondary endpoints are overall response rate, duration of response, time to progression, progression free survival and overall survival. Main eligibility criteria include age ≥18, KPS ≥60, GBM at first or second relapse with a measurable lesion on ≤2mg dexamethasone. This is the first clinical trial to investigate CYNK-001 in GBM and will lay the foundation for future NK cell therapy in solid tumors.

RTID-08. A PHASE 1/2 STUDY OF SELINEXOR IN COMBINATION WITH STANDARD OF CARE THERAPY FOR NEWLY DIAGNOSED OR RECURRENT GLIOBLASTOMA (NDGBM OR RGBM)

Patrick Wen[1], Yazmin Odia[2], Minesh Mehta[2], Samuel Goldlust[3], Sharon Tamir[4], Sharon Shacham[4], Hongwei Wang[4], Heidi Sheehan[74] and Kai Li[4]; [1]Dana-Farber Cancer Institute, Boston, MA, USA, [2]Miami Cancer Institute, Miami, FL, USA, [3]Hackensack University Medical Center, Hackensack, NJ, USA, [4]Karyopharm Therapeutics, Inc., Newton, MA, USA

BACKGROUND: GBM is the most common and most aggressive primary brain tumor with poor prognosis and median overall survival (mOS) of patients with ndGBM and rGBM being 15 vs 5-7 months, respectively. Selinexor is a first-in class, oral, selective nuclear export inhibitor which forces nuclear retention and reactivation of many tumor suppressor proteins. Selinexor with low dose dexamethasone was recently approved for patients with triple-class refractory multiple myeloma. Additionally, selinexor monotherapy has demonstrated broad activity in other hematologic and solid malignancies. In a Phase 2 study in rGBM (NCT01986348), selinexor demonstrated encouraging intratumoral penetration and single-agent efficacy at 80 mg once weekly with durable response and disease stabilization in heavily pretreated patients. Preclinical GBM studies showed synergy when combining selinexor with radiation, temozolomide and lomustine. METHOD: This is a phase 1 (PH-1) dose finding study followed by a 1:1 randomized phase 2 (PH-2; n= 350) efficacy exploration trial to independently evaluate 3 different combination regimens: Arm A: radiation +/- selinexor in uMGMT ndGBM; Arm B: radiation and temozolomide +/- selinexor in MGMT ndGBM; Arm C:omustine +/- selinexor in first relapse rGBM following frontline radiation and temozolomide. The PH-1 primary endpoint is MTD/RP2D, with secondary endpoints of ORR per modified RANO, duration of response (DOR), PFS, and OS. The PH-2 primary endpoint for Arms A and B in ndGBM is PFS, with key secondary endpoints being OS, PFS6, ORR, DOR. For Arm C, the PH-2 primary endpoint is OS while key secondary endpoints are PFS, PFS6, ORR, DOR. The study has 70% power to detect a hazard ratio of 0.67 between selinexor and control for primary efficacy for arms A & B, and 80% power to detect a hazard ratio of 0.70 for arm C. We are currently enrolling patients nationwide. Clinical trial identifier: NCT04421378

RTID-09. A RANDOMIZED, DOUBLE-BLINDED, PHASE 3 STUDY OF ENZASTAURIN ADDED TO TEMOZOLOMIDE DURING AND FOLLOWING RADIATION THERAPY IN NEWLY DIAGNOSED GLIOBLASTOMA PATIENTS WHO POSSESS THE NOVEL BIOMARKER, DGM1

Nicholas Butowski[1], Ying Mao[2], Wilson Wu[3], Wen Luo[3], Lan Ge[4], Daniel Pertschuk[5], Theresa Dewitt[3], Isabel Han[4], and Thomas Heineman[3]; [1]University of California San Francisco, San Francisco, CA, USA, [2]Fudan University, Shanghai, China (People's Republic), [3]Denovo Biopharma, San Diego, CA, USA, [4]Denovo Biopharma, Beijing, China (People's Republic), [5]Consultant Oncologist, Solana Beach, CA, USA

BACKGROUND: Limited progress has been made in improving therapeutic outcomes for glioblastoma (GBM) patients. Enzastaurin (enza) is an oral PKC-β inhibitor that suppresses signaling through the PKC and PI3K/AKT pathways. Although enza did not significantly improve survival in a prior Phase 1/2 study, we have identified a novel genomic biomarker, DGM1, that may predict a response to enza in GBM. PRIMARY OBJECTIVE: To assess whether enza added to temozolomide and radiation therapy (RT) improves overall survival (OS) in newly diagnosed GBM patients who possess the DGM1 biomarker. POPULATION: Adults with newly diagnosed GBM regardless of DGM1 status who have undergone surgical resection and are candidates for chemoradiation. Approximately 318 patients will be enrolled. DGM1 status will be determined prior to analysis. DESIGN: This is a randomized, double-blinded, placebo-controlled study. Patients will be stratified by MGMT and IDH1 status and by geographic region. Treatment will be divided into 3 phases. In the Concurrent Phase (6 weeks), patients will receive RT plus temozolomide and either enzastaurin or placebo. Patients will then enter the Single-Agent Phase and receive either enza or placebo (21-35 days). Then, patients will enter the Adjuvant Phase and receive temozolomide with either enza or placebo (6-12 cycles) followed by enza or placebo alone (to 24 cycles total). ANALYSIS: The primary efficacy endpoint of OS will be analyzed using stratified log-rank test for all DGM1-positive randomized patients. The study has approximately 90% power to detect a HR of 0.63 assuming 196 OS events based on a 2.5% one-sided false positive error rate. Statistical significance would be achieved with an estimated observed HR < 0.76. Safety evaluation will include all patients receiving at least one dose of enza or placebo. If OS in DGM1-positive patients is statistically significant, OS in the overall population will be assessed.

RTID-10. SURGEONS TRIAL OF PROPHYLAXIS FOR EPILEPSY IN SEIZURE NAÏVE PATIENTS WITH MENINGIOMA: A RANDOMIZED CONTROLLED TRIAL (STOP 'EM)

Michael Jenkinson[1], Adel Helmy[2], Helen Huckey[1], Samantha Mills[3], Robin Grant[4], Dyfrig Hughes[5], Tony Marson[1], Rebecca Tangney[6], Helen Bulbeck[7], Usama Ali[8], and Carrol Gamble[1]; [1]University of Liverpool, Liverpool, United Kingdom, [2]Addenbrookes Hospital, Cambridge, United Kingdom, [3]The Walton Centre, Liverpool, United Kingdom, [4]NHS Lothian, Edinburgh, United Kingdom, [5]University of Bangor, Bangor, United Kingdom, [6]Royal Liverpool Hospitals, Liverpool, United Kingdom, [7]Brainstrust, Isle of White, USA, [8]University of Oxford, Oxford, United Kingdom

BACKGROUND: Meningioma is the commonest primary brain tumour. 70% of patients are seizure-free at presentation, but approximately 12% will have seizures within 12 months of surgery. Seizures impact quality of life. Neurosurgeons administer prophylactic anti-epileptic drugs (AED) to prevent seizures despite a lack of evidence to support this. A meta-analysis of RCTs in brain tumours suggests that older AED may prevent seizures in the first week after surgery but not thereafter. There are no studies assessing newer AEDs in the prophylactic setting. RESEARCH QUESTION: In patients with meningioma who have never had a seizure and are undergoing surgical resection, does prophylactic levetiracetam reduce the risk of developing seizures? DESIGN: multi-centre, double-blind RCT in 20 UK centres. 1:1 randomisation of 14 days levetiracetam 500mg bd started one day before surgery compared to placebo. PRIMARY OBJECTIVE: Determine whether 2 weeks prophylactic levetiracetam reduces the risk of developing seizures within 12 months of surgery compared to placebo. ECONOMIC OBJECTIVE: Estimate cost-effectiveness of prophylactic levetiracetam. SECONDARY OBJECTIVES: Determine effect of prophylaxis on time to first seizure and first convulsive seizure, whether prophylaxis affects quality of life and influences return to driving, safety of prophylaxis. POPULATION: seizure-naïve meningioma undergoing surgery. SAMPLE SIZE: seizure rate at 12 months is 12.3%. A 50% reduction is clinically beneficial. A two-group chi-squared test with 5% two-sided significance level will have 90% power to detect the difference between a Group 1 proportion of 0.12 and a Group 2 proportion of 0.06 when the sample size in each group is 477. Allowing for 5% dropout, 1004 patients will be recruited. FUNDING: NIHR (£1.64M) award June 2020. Study opens March 2021. TRANSLATIONAL RESEARCH: MRI, blood and tissue will be collected to explore risk factors for seizures. CONCLUSIONS: study will provide class I evidence of the role of prophylactic levetiracetam in meningioma surgery.

RTID-11. GBM AGILE: A GLOBAL, PHASE 2/3 ADAPTIVE PLATFORM TRIAL TO EVALUATE MULTIPLE REGIMENS IN NEWLY DIAGNOSED AND RECURRENT GLIOBLASTOMA

Meredith Buxton[1], Brian Alexander[2], Donald Berry[3], Webster Cavenee[4], Howard Colman[5], John de Groot[6], Benjamin Ellingson[7], Gary Gordon[8], Mustafa Khasraw[9], Andrew Lassman[10], Wenbin Lee[11], Michael Lim[12], Ingo Mellinghoff[13], James Perry[14], Erik Sulman[15], Kirk Tanner[16], Michael Weller[17], Patrick Wen[18], W K Alfred Yung[19], Timothy Cloughesy[7], and GBM AGILE Investigators[20]; [1]Global Coalition for Adaptive Research, Los Angeles, CA, USA, [2]Dana-Farber Cancer Institute, Boston, MA, USA, [3]University of Texas M.D. Anderson Cancer Center, Houston, TX, USA, [4]University of California San Diego, San Diego, CA, USA, [5]Huntsman Cancer Institute, Salt Lake City, UT, USA, [6]University of Texas MD Anderson Cancer Center, Houston, TX, USA, [7]University of California Los Angeles, Los Angeles, CA, USA, [8]Global Coalition for Adaptive Research, Chicago, IL, USA, [9]Duke University, Durham, USA, [10]New York Presbyterian Hospital/Columbia University Irving Medical Center, New York, NY, USA, [11]Tiantan Hospital, Capital Medical University, Beijing, China (People's Republic), [12]Johns Hopkins University School of Medicine, Baltimore, MD, USA, [13]Memorial Sloan Kettering Cancer Center, New York, NY, USA, [14]Sunnybrook Health Sciences Centre, Toronto, ON, Canada, [15]Department of Radiation Oncology at NYU Grossman School of Medicine, New York, NY, USA, [16]National Brain Tumor Society, Newton, MA, USA, [17]UniversitätsSpital Zürich - Klinik für Neurologie, Zurich, Switzerland, [18]Dana-Farber Cancer

Institute, Boston, MA, USA, [19]MD Anderson Cancer Center, Houston, TX, USA, [20]GBM AGILE Investigators, Los Angeles, CA, USA

Developing new therapies for patients with glioblastoma (GBM) requires focused interaction between industry, academia, nonprofits, patient advocacy, and health authorities, and novel approaches to clinical trials. GBM *A*daptive *G*lobal *I*nnovative *L*earning *E*nvironment (GBM AGILE) Trial was designed by over 130 global key opinion leaders in consultation with health authorities to provide an optimal mechanism for phase 2/3 development in GBM. The Sponsor of GBM AGILE is the Global Coalition for Adaptive Research, whose mission is to accelerate the development of treatments rare and deadly diseases by serving as sponsor of innovative trials. GBM AGILE is an international platform trial designed to evaluate multiple therapies in newly diagnosed and recurrent GBM. Its goals are to identify effective therapies for GBM and match effective therapies with patient subtypes, with data generated to support regulatory filing for new drug applications. Bayesian response adaptive randomization is used within subtypes of the disease to assign participants to investigational arms based on their performance. The primary endpoint is overall survival. The trial is being conducted under a master Investigational New Drug Application/Clinical Trial Agreement and Master Protocol, allowing multiple drugs from different companies to be evaluated simultaneously and/or over time. The plan is to add experimental therapies as new information is identified and remove therapies as they complete their individual evaluation against a common control. GBM AGILE received IND approval from the FDA in April 2019, screening its first patient in June 2019. As of June 2020 over 200 patients have been screened. Expansion to Canada, Europe, China, and Australia is also underway. There is currently one investigational arm under evaluation in the trial, with two additional arms to be added in Q4 2020/ Q1 2021. Clinical trial information: NCT03970447.

RTID-12. PHASE 2 TRIAL OF TUMOR TREATING FIELDS (TTFIELDS) PLUS RADIATION THERAPY (RT) PLUS TEMOZOLAMIDE (TMZ) COMPARED TO RT PLUS TEMOZOLOMIDE IN NEWLY DIAGNOSED GLIOBLASTOMA (NDGBM)

Rachel Grossman, Dror Limon, Felix Bokstein, Carmit Ben Harosh, Deborah Blumenthal, and Zvi Ram; Tel Aviv Medical Center, Tel Aviv, Israel

OBJECTIVE: In the EF-14 phase 3 trial, TTFields 9200 kHz) added to maintenance TMZ increased median OS to 20.9 months versus 16.0 months with maintenance TMZ ($p< 0.001$) in ndGBM. Preclinical investigations showed that TTFields/RT have a synergistic effect. A pilot study (N=10) in ndGBM demonstrated the feasibility and safety of TTFields combined with RT/TMZ (Grossman Front Onc 2020). The only TTFields-related adverse event was array-associated skin toxicity. Median PFS was 8.9 months. Based on these encouraging results, this prospective, randomized phase 2 study [NCT03869242] in 60 patients further investigates if the addition of TTFields TMZ/RT treatment in ndGBM patients improves treatment efficacy and delays disease progression. METHODS: Following debulking surgery or biopsy, 60 patients (≥18 years) with histologically confirmed GBM, KPS≥70 and life expectancy >3 months will be randomized 1:1 to: i) RT with concomitant TMZ/TTFields (200 kHz) for 6 weeks followed by up to 6 months of maintenance TMZ combined with TTFields (experimental arm) up to 24 months; ***or*** ii) RT with concomitant TMZ alone followed by maintenance TMZ combined with TTFields (control arm). Patients with early progressive disease, significant comorbidities precluding maintenance RT or TMZ or with implanted electronic devices will be excluded. The primary endpoint is the rate of progression free survival at 12 months (PFS12). Treatment with TTF will be continued until second progression or 24 months (the earlier of the two). All patients will be followed for survival. All adverse events will graded per CTCAE V5.0. The sample size of 60 patients provides 80% power with two-sided alpha level of 0.05 to detect a PFS12 of 46.5% with RT/TMZ/TTFields compared to 29.4% with RT/TMZ followed, respectively, by maintenance TMZ/TTFields (calculated from the RT/TMZ followed by maintenance TMZ/TTFields arm of the EF-14 trial). Follow-up will continue for >12 months from recruitment of the last patient.

CANCER STEM CELLS

STEM-01. TARGETING BRAIN METASTASIS-INITIATING CELLS: A PREVENTATIVE APPROACH

Agata Kieliszek[1], Chitra Venugopal[2], Blessing Bassey-Archibong[1], Fred Lam[2], Sheila Singh[2], and Nikoo Aghaei[1]; [1]McMaster University, Mississauga, ON, Canada, [2]McMaster University, Hamilton, ON, Canada

BACKGROUND: The incidence of brain metastases (BM) is tenfold higher than primary brain tumors. BM commonly originate from primary lung, breast, and melanoma tumors with a 90% mortality rate within one year of diagnosis. Current standard of care for BM includes surgical resection with concurrent chemoradiation, but does not extend median survival past 16 months, posing a large unmet need to identify novel therapies against BM. METHODS: From a large in-house biobank of patient-derived BM cell lines, the Singh Lab has generated murine orthotopic patient-derived xenograft (PDX) models of lung, breast, and melanoma BM that recapitulate the stages of BM progression as seen in humans. Using these three PDX models, we identified a population of "pre-metastatic" brain metastasis-initiating cells (BMICs) that are newly arrived in the brain but have yet to form detectable tumors. Pre-metastatic BMICs are not detectable in human patients but are important therapeutic targets with the potential to prevent BM in at-risk patients. RESULTS: RNA sequencing of pre-metastatic BMICs from all three PDX primary tumor models with subsequent Connectivity Map analysis identified novel compounds that have the potential of killing all three types of BMICs. In particular, we identified two compounds that have selective killing of BMICs in vitro from all three primary tumor cohorts while sparing non-cancerous cells. We further characterized their ability to inhibit the self-renewal and proliferative properties of BMICs. Ongoing in vivo work will investigate the compounds' preclinical utilities in preventing BM. CONCLUSION: Identification of novel small molecules that target BMICs could prevent the formation of BM completely and dramatically improve the prognosis of at-risk cancer patients.

STEM-02. IN VIVO PHAGE DISPLAY IDENTIFIES PEPTIDE TARGETING N-CADHERIN ON GLIOMA STEM CELLS

Marine Potez[1], Jongmyung Kim[1], Chunhua She[1], Neelkamal Chaudhary[1], and James Liu[2]; [1]Moffitt Cancer Center, Tampa, FL, USA, [2]H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL, USA

Glioblastoma (GBM) is the most aggressive primary brain tumor with high mortality rates and resistance to conventional therapy. Glioma stem cells (GSCs) comprise a sub-population of glioma tumor cells with the ability of self-renewal and tumor recapitulation, and may be responsible for GBM's treatment resistant properties. Identification of surface receptors that are novel and specific to GSCs may be the key to the development of effective therapeutic strategies. We have selected a GSC specific targeting peptide isolated through *in vitro* and *in vivo* phage display biopanning. This screening technique allowed us to determine a peptide (GBM-IC2) which binds specifically to GSCs *in vitro*, and to GBM tissue *in vivo*. Although this screening process allows for isolation of cell specific targeting peptides, it does so without identification of the cellular binding partner. Given the specificity of the peptide, identification of the cellular receptor may allow for discovery of novel markers to identify GSCs. To identify the peptide binding partner of GBM-IC2, the biotinylated peptide was incubated with GSC protein lysate. The peptide, along with its binding partner, was isolated using streptavidin agarose resin. The binding partner protein was then identified using mass spectroscopy. This revealed N-cadherin (CDH2) as a potential binding partner for the GBM-IC2 peptide. GBM-IC2 demonstrated specificity for targeting CDH2 compared to control peptide using ELISA. Lentiviral induced overexpression of CDH2 in HEK293 cells allowed for GBM-IC2 peptide binding. Competition assay was performed by applying anti-CDH2 antibody to GBM-IC2 peptide and GSCs in culture. Application of anti-CDH2 antibody decreased peptide binding to GSCs, confirming CDH2 as the binding partner for GBM-IC2. These results demonstrate that cell specific targeting peptides isolated through phage display may lead to the isolation of novel cell specific proteins through immunoprecipitation isolation and mass spectroscopy analysis.

STEM-03. WAVE1 KNOCKDOWN ENHANCES THE ANTITUMOR EFFICACY IN PRIMARY GLIOBLASTOMA NEUROSPHERES

Sriya Namagiri[1], Shilpa Thammegowda[2], Hannah Sur[1], Amélie Vézina[1], Ashis Chowdhury[1], Dragan Maric[3], Arunakumar Gangaplara[4], Nancy Edwards[1], Sadhana Jackson[1], Abhik Ray-Chaudhury[1], John Heiss[1], and Yeshavanth Kumar Banasavadi-Siddegowda[1]; [1]Surgical Neurology Branch, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD, USA, [2]Department of Veterinary Pathology, Veterinary College, KVAFSU, Hassan, Karnataka, India, [3]Flow and Imaging Cytometry Core Facility, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD, USA, [4]Cellular and Molecular Therapeutics Branch, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD, USA

INTRODUCTION: Despite multi-model therapies that include maximal surgical resection, radiation, chemotherapy, and tumor treating fields, the median survival of Glioblastoma (GBM) patients is around 15 months. WASP-family verprolin homologous protein 1 (WAVE1) is a downstream effector that receives signals from small GTPases to regulate the actin cytoskeleton. WAVE1's interaction with arp2/3 modulates critical roles, such as cell motility and morphologic changes. Expression of WAVE1 has been implicated in leukemia, ovarian, and prostate cancer. In this study, we