SPCR-02

NEUROCOGNITIVE FUNCTION IN PATIENTS WITH LEPTOMENINGEAL METASTASIS TREATED WITH PROTON CRANIOSPINAL IRRADIATION

Denise Correa, Adrian Koch, Raymond Baser, Elena Pentsova, Suzanne Wolden, Brandon Imber, Adrienne Boire, Jonathan Yang; Memorial Sloan Kettering Cancer Center, New York, NY, USA

BACKGROUND: Proton craniospinal irradiation (pCSI) as a potential treatment for patients with solid tumor leptomeningeal metastasis (LM) is being assessed in a phase II randomized study comparing it with photon involved-field radiotherapy (RT). We report the preliminary results of prospective neurocognitive function in a subset of patients treated with pCSI. METHODS: Patients with LM and without evidence of CNS disease progression completed standardized neurocognitive tests of attention and working memory, executive function, and verbal memory at baseline (pre-pCSI), and 3 and 6 months post-pCSI. All patients received chemotherapy (baseline and follow up) and memantine (follow up). Means across the three timepoints were estimated for each neurocognitive test score using a linear mixed model (LMM) predicting the score by timepoint. Mean changes between pairs of timepoints were similarly estimated from the LMMs and tested for statistical significance using model-based contrasts. RESULTS: Baseline, 3-month and 6-month neurocognitive data were available for 12, 11, and 8 patients, respectively. Linear mixed model analyses showed a significant decline in graphomotor speed (Trails A, p=0.03), verbal learning (HVLT-R Total Learning, p<0.001), and verbal recognition memory (HVLT-R Discrimination, p=0.03) from baseline to 3 months post-pCSI, with scores remaining stable at 6 months post-pCSI. There was a significant decline in timed set-shifting (Trails B, p=0.04) from baseline to 6 months post-pCSI. There were no significant changes in attention and working memory over the follow-up period. CONCLUSION: Preliminary results in a subset of patients showed a decline in graphomotor speed and verbal memory at 3 months and executive function at 6 months post-pCSI, possibly related to the early adverse effects of RT. These results are overall consistent with findings in other populations treated with whole-brain RT. However, there was no change in attention and working memory and most cognitive domains remained stable at six months with pCSI.

SPCR-03

NEUROCOGNITIVE OUTCOMES FROM PHASE 1 TRIAL OF BMX-001 IN COMBINATION WITH CONCURRENT RADIATION THERAPY AND TEMOZOLOMIDE IN NEWLY DIAGNOSED HIGH-GRADE GLIOMA PATIENTS

Katherine Peters[1], John Kirkpatrick[1], Ines Batinic-Haberle[1], Mary Lou Affronti[1], Sarah Woodring[1], Eric Lipp[1], James Herndon[1], Kendra Boyd[1], Ivan Spasojevic[1], Sara Penchev[2], Shayne Gad[3], David Silberstein[2], Margaret Johnson[1], Annick Desjardins[1], Henry Friedman[1], David Ashley[1], James Crapo[2]; [1]Duke University Medical Center, Durham, NC, USA. [2]BioMimetix JV, LLC, Greenwood Village, CO, USA. [3]Gad Consulting, Durham, NC, USA

INTRODUCTION: Neurocognitive dysfunction can result from radiation therapy which is the mainstay of treatment for high-grade glioma, particularly glioblastoma. Preclinical observations found that BMX-001, a novel metalloporphyrin, acts as a radioprotectant for normal CNS cells yet as a radiosensitizer to cancer cells in human GBM xenograft experiments. In a phase 1 study evaluating the safety of BMX-001 in combination with concurrent radiation therapy and temozolomide, we further studied neurocognitive function before and after concurrent radiation therapy and temozolomide in newly diagnosed high-grade glioma patients. METHODS: We performed a phase 1 study of BMX-001 combined with radiation therapy (6-week total of 59.4-60 Gy) and temozolomide (75 mg/m2/day for 42 days). We administered BMX-001 as a subcutaneous injection at a loading dose before radiation therapy and temozolomide and then subsequent doses twice weekly for eight weeks. A key secondary endpoint was the evaluation of neurocognition. We performed neurocognitive testing with the computerized program CNS Vital Signsâ. This battery consists of seven tests: verbal memory, visual memory, finger tapping, symbol digit coding, the Stroop Test, a test of shifting attention, and a continuous performance test. We defined neurocognitive impairment at baseline as a z-score ≥ 1.5 SDs below the normative mean. We described improvements or declines in neurocognition at 2 and 6 months from baseline. RESULTS: Fifteen patients (age 19-80 years) enrolled and underwent neurocognitive testing before and after RT. All patients had WHO grade 4 glioblastoma. Most subjects had neurocognitive impairment ranging from 46.7-to 80% on specific neurocognitive tests. At two months (N=15) and six months (N=9), most testing demonstrated improved neurocognitive performance. CONCLUSIONS: Neurocognitive function is maintained and can improve after concurrent radiation therapy and temozolomide in this high-grade glioma cohort treated with BMX-001 during concurrent radiation therapy and temozolomide.

SPCR-04

EFFECTS OF BRAIN METASTASES ON NEUROCOGNITIVE FUNCTION: BASELINE RESULTS OF A LONGITUDINAL TRIAL

Randa Higazy[1,2], Matthew Ramotar[1], Zhihui Amy Liu[3,2], Anna T. Santiago[3], Natalya Kosyak[1], Geoffrey Liu[4,2], Rebecca Simpson[5], David B. Shultz[1,2], Kim Edelstein[5,2]; [1]Radiation Medicine Program, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada. [2]University of Toronto, Toronto, ON, Canada. [3]Department of Biostatistics, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada. [4]Department of Medical Oncology and Hematology, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada. [5]Department of Supportive Care, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada

PURPOSE: Neurocognitive dysfunction is common in patients with advanced metastatic cancer. The contribution of brain metastases (BrMets) to neurocognitive outcomes is uncertain. We examined the impact of BrMets on cognitive outcomes before CNS-directed treatment and compared findings to patients with advanced metastatic cancer without BrMets. Here we present results from an ongoing prospective, longitudinal study. METHODS: English-speaking adults followed at the brain metastases and lung cancer clinics underwent neurocognitive testing using a standardized battery (prior to cranial radiotherapy, if applicable), with follow-up assessments 3, 6, 9, 12, 18, and 24 months later. We calculated z-scores and impairment rates for composite neurocognitive function and memory, attention/working memory, processing speed and executive function domains. Impairment was defined according to International Cancer and Cognition Task Force criteria. RESULTS: 78 patients with BrMets (50% female; mean age (SD):61(11) years) and 28 patients with metastatic non-small cell lung cancer (mNSCLC) with no known BrMets (71% female; age 67(9) years) were included. Baseline neurocognitive composite scores were impaired in both groups (BrMets: 61.5%; nonBrMets: 60.7%). Impairment rates varied between groups and across domains (BrMets vs nonBrMets: memory: 35.9%vs25.0%; attention/working memory: 35.8%vs21.4%; processing speed: 10.3%vs7.1%; executive function: 44.0%vs35.7%). Subgroup comparisons between BrMets patients with mNSCLC (N=29) and mNSCLC patients without BrMets, none of whom had targetable mutations, revealed no differences in impairment rates, but BrMets patients had slower processing speed than nonBrMets patients (mean(SD): -0.6(1.4) vs -0.1(1.9); Wilcoxon signed-rank test, p = 0.043). CONCLUSION: Neurocognitive impairment in patients with advanced cancers is common. Our preliminary findings demonstrate no clear difference in cognitive outcomes between patients with BrMets and those with advanced metastatic disease not involving the brain. Our work examining how neurocognitive outcomes evolve over time in patients with and without BrMets, and demographic, disease, and treatment variables associated with those outcomes, is ongoing.

FINAL CATEGORY: SYSTEMIC THERAPEUTICS

SYST-01

MULTI-INSTITUTIONAL RANDOMIZED TRIAL COMPARING CANCER STEM CELL-TARGETED VS PHYSICIAN-CHOICE TREATMENTS IN PATIENTS WITH RECURRENT HIGH-GRADE GLIOMAS (NCT03632135)

Soma Sengupta[1], Tulika Ranjan[2], Alexander Yu[3], Candace Howard[4], Ricky Chen[5], Rekha Chaudahary[1], Nicholas Marko[1], Darit Aregawi[6], Michael Glantz[6], Jon Glass[7], Richard Green[8], Christine Lu-Hemerson[9], Aaaron Mammoser[10], Hugh Moulding[11], Steven Jubelirer[12], Jason Schoroeder[13], Mark Anderson[4], Frances Chow[14], Seth Lirette[4], Krista Denning[15], Anthony Alberico[15], Jagan Valluri[15], Pier Paolo Claudio[16]; [1]University of Cincinnati, Cincinnati, OH, USA. [2]Tampa General Hospital, Tampa, FL, USA. [3]Allegheny Health Network, Pittsburgh, PA, USA. [4]University of Mississippi Medical Center, Jackson, MS, USA. [5]Providence Brain & Spine Institute, Providence, WA, USA. [6]Penn State Neuroscience Institute, Hershey, PA, USA. [7]Thomas Jefferson University, Philadelphia, PA, USA. [8]Southern California Permanente Medical Group, Los Angeles, CA, USA. [9]Maine Medical Center, Scarborough, ME, USA. [10]Louisiana State University, New Orleans/ LA, USA. [11]St. Luke's University Health Network, Bethlehem, PA, USA. [12]Charleston Area Medical Center, Charleston, WV, USA. [13]University of Toledo, Toledo, OH, USA. [14]University of Southern California, Los Angeles, CA, USA. [15]Marshall University, Huntington, WV, USA. [16]University of Mississippi, Jackson, MS, USA

BACKGROUND: Clinical outcomes in patients with recurrent high-grade glioma (HGG) remain poor. Cancer stem cells (CSCs) have been implicated in metastasis, treatment resistance and recurrence of HHGs. We have shown in several clinical studies that anti-CSC-directed therapy provides benefits in many cancer types; however, this is the first report of a randomized clinical