8-9-2021

PARP Inhibitor Tolerability and Impact on Progression-Free Survival in Patients with High-Grade, Ovarian Carcinoma with Brain Metastasis: A Case-Series

Alexander Mohler
Miami Cancer Institute, alexandermo@baptisthealth.net

Belkys Salinas
Miami Cancer Institute, BelkysAS@baptisthealth.net

Rupesh Kotecha
Miami Cancer Institute, rupeshk@baptisthealth.net

Karissa Nazur
Miami Cancer Institute, KarissaL@baptisthealth.net

Yazmin Odia
Miami Cancer Institute, yazmino@baptisthealth.net

See next page for additional authors

Citation

Neuro-Oncology Advances, Volume 3, Issue Supplement_3, August 2021, Pages iii12–iii13,

Authors
Alexander Mohler, Belkys Salinas, Rupesh Kotecha, Karissa Nazur, Yazmin Odia, and Nicholas Lambrou

of LMD is largely devoid of CD3+ T cells, but is enriched for immune suppression and innate immunity.

LMD-21. HEADACHE IMPROVEMENT PREDICTS SURVIVAL AFTER CSF DIVERSION IN LEPTOMENINGEAL DISEASE

Adam Robin[1], Sameah Haider[1], Natalie Distefano[2], Anne Reiner[2], Viviane Tabar[2], Jacob Pawloski[3]; [1]Henry Ford Health System, Detroit, MI, USA, [2]Memorial Sloan Kettering Cancer Center, New York, NY, USA, [3]Henry Ford Health Center, Detroit, MI, USA

BACKGROUND: Leptomeningeal carcinomatosis (LMD) is a seeding of the leptomeninges by malignant cells. Clinical, treatment and patient-related factors have been described in patients with LMD. Current data are limited by small sample size, particularly in patients undergoing ventriculoperitoneal shunting (VPS) as part of the treatment regimen. OBJECTIVE: This study presents the largest cohort of LMD patients in the literature undergoing cerebrospinal fluid (CSF) diversion and seeks to identify prognostic factors related to survival. METHODS: A retrospective review of patients diagnosed with LMD between 2010 and 2016 at a quaternary referral center was performed. Cox proportional hazards modeling was utilized to identify variables associated with improved overall survival from LMD diagnosis. Overall survival was depicted using Kaplan-Meier methodology. Competing risk methodology was used to identify variables associated with VPS, considering death as a competing event. RESULTS: Of the 314 patients identified, 112 underwent VPS placement. The median overall survival from LMD diagnosis was 3.9 months (95% CI: 3.2–4.4). The presence of headaches, increased opening pressure, and gait difficulty increased the likelihood of VPS placement (all $p<0.05$). VPS, older age, lower Karnofsky Performance Status (KPS), higher opening pressure and CSF nucleated cell count (NCC) increased the risk of death (all $p<0.05$). Patients reporting headache improvement after VPS had better survival ($p<0.05$). CONCLUSIONS: Headache, increased opening pressure and gait instability were associated with higher rate of VPS placement and may portend more aggressive disease. Headache improvement following VPS is a favorable prognostic sign, suggesting survival advantage for patients with hydrocephalus undergoing VPS. Age, KPS, VPS, opening pressure, CSF NCC, concomitant visceral metastases and histology-specific molecular profile impact survival.

LMD-22. CLINICOPATHOLOGICAL SPECTRUM OF LEPTOMENINGEAL METASTASES: A 3 YEAR RETROSPECTIVE STUDY

Saloni Pahwa, Anila Sharma, Meenakshi Kamboj, Anurag Mehta; RGCIRC, Delhi, India

OBJECTIVES: Cytological examination of cerebrospinal fluid is a widely used cost effective, simple procedure and a reliable routine diagnostic test. CSF cytology helps in detection of inflammatory diseases of the CNS, diagnosis of subarachnoid haemorrhage and the identification of malignant cells in metastatic or rarely primary CNS malignancies.Leptomeningeal metastases (LM) is estimated to occur in 5% of all patients with cancer. It has a higher propensity to occur in solid tumours compared to haematological malignancies.In view of poor prognosis, early diagnosis may aid in appropriate tumour staging and aggressive therapeutic intervention. METHODS: All the samples of CSF received in the Department of Laboratory for cytological examination and reported as 'positive for malignant cells' during the year January 2018 to December 2020were included in the study. All the cases were routinely evaluated on Neubauer's chamber, direct smear and a cytospin preparation stained using MGG stain. The clinical records and any further ancillary testing performed were retrospectively analysed. RESULTS: 87cases with LM were identified over 3 year duration. Mean age of presentation was 43 years. Metastatic solid malignancies (56%) had a higher incidence of leptomeningeal metastases compared to haematolymphoid malignancies (40%) and CNS medulloblastomas(2%). Most common solid tumour with involvement of CSF was adenocarcinoma lung (51%) followed by breast carcinoma (37%). Of all the cases of adenocarcinoma lung with LM, EGFR mutant NSCLC were 40% while 8% showed ALK gene rearrangement. Amongst the haematological malignancies, acute leukaemia's constituted 67% of cases while systemic NHLs were 34%. Most of the cases (97%) presented with neurological symptoms during the course of treatment while 3 cases (3%) showed LM at the time of first presentation. CONCLUSIONS: With appropriate clinicoradiological correlation, CSF cytology remains the gold standard for identification of malignant cells in cases with already known primary tumour (leptomeningeal dissemination of the disease). In this study, clinical features of both solid and haematolymphoid malignancies were evaluated. The group of solid malignancies included adenocarcinomas lung, breast, gastrointestinal tract and renal cell carcinoma. With the availability of EGFR TKIs and ALK inhibitors, overall survival of the patients may be prolonged with therapeutic interventions despite limited CSF and CNS penetration of these drugs.

MEDICAL THERAPY (CHEMOTHERAPY AND IMMUNOTHERAPY)

THER-01. TARGETED THERAPY AND INTRACRANIAL METASTATIC DISEASE: A POPULATION-BASED RETROSPECTIVE COHORT STUDY

Anders Erickson[1], Steven Habbous[2], Frances Wright[3], Aisha Lofters[4], Katarzyna Jerzak[5], Sunit Das[1,6]; [1]Institute of Medical Science, Faculty of Medicine, University of Toronto, Toronto, ON, Canada, [2]Ontario Health (Cancer Care Ontario), Toronto, ON, Canada, [3]Division of General Surgery, Department of Surgery, Sunnybrook Hospital, University of Toronto, Toronto, ON, Canada, [4]Department of Family & Community Medicine, University of Toronto, Women's College Hospital, Toronto, ON, Canada, [5]Department of Medicine, Sunnybrook Odette Cancer Centre, University of Toronto, Toronto, ON, Canada, [6]Division of Neurosurgery, Department of Surgery, St. Michael's Hospital, University of Toronto, Toronto, ON, Canada

BACKGROUND: Targeted therapies have been hypothesized to prolong survival in the management of patients with intracranial metastatic disease (IMD), but, paradoxically, to increase IMD incidence by improving systemic disease control and prolonging survival from the primary tumor. The real-world benefits of targeted therapy in management of patients with IMD are unclear, as clinical trials have excluded patients with IMD and lacked endpoints reporting intracranial outcomes. METHODS: This retrospective cohort study included all patients in Ontario, Canada, diagnosed with IMD from 2005 to 2018 with primary diagnoses of breast cancer, lung or bronchus cancer, or melanoma, and control patients matched by primary disease without IMD. Kaplan-Meier and multivariable Cox regression analyses were performed to compare overall survival (OS) between patient subcohorts divided by primary disease and stratified by targeted therapy receipt or IMD status. RESULTS: Post-IMD targeted therapy was associated with prolonged OS in patients with HER2-positive breast cancer (HR 0.41; 95% CI, 0.33–0.5), EGFR-positive lung cancer (HR 0.28; 95% CI, 0.23–0.34), and BRAF-positive melanoma (HR 0.2; 95% CI, 0.14–0.29), compared to those who did not receive post-IMD targeted therapy. Presence of IMD was associated with shorter OS in patients with metastatic HER2-positive breast cancer (HR 1.8; 95% CI, 1.56–2.08) and metastatic EGFR-positive lung cancer (HR 1.22; 95% CI, 1.08–1.39) but not metastatic BRAF-positive melanoma (HR 1.11; 95% CI, 0.77–1.61), compared to those without IMD. CONCLUSIONS: Our findings show that real-world use of targeted therapies was associated with prolonged OS in patients with IMD in the setting of HER2-positive breast cancer, EGFR-positive lung cancer, and BRAF-positive melanoma. Inclusion of patients with IMD in clinical trials and use of endpoints that interrogate IMD will be critical to determine the role of targeted therapies in the management of patients with IMD.

THER-02. PARP INHIBITOR TOLERABILITY AND IMPACT ON PROGRESSION-FREE SURVIVAL IN PATIENTS WITH HIGH-GRADE, OVARIAN CARCINOMA WITH BRAIN METASTASIS: A CASE-SERIES

Alexander Mohler[1], Belkys Salinas[2], Karissa Nazur[2], Yazmin Odia[2], Nicholas Lambrou[2]; [1]Miami Cancer Institute, Miami, FL, USA, [2]Miami Cancer Institute, Miami, FL, USA

Brain metastases secondary to ovarian carcinoma is an uncommon but increasing phenomenon. PARP inhibitors (PARPi) are increasingly used as an adjunctive treatment in patients with central nervous system metastases (CNS). Historically brain metastases has a historically poor prognosis. Five women with a mean age of 60.4 ± 7.6 years were included. All had stage IIIC/IV ovarian cancer and diagnosed with brain metastases at recurrence. Three underwent resection for oligometastatic disease followed by post-operative stereotactic radiosurgery (SRS), one had SRS without surgery, and one patient underwent whole brain radiotherapy for multiple metastases. Pathology was confirmed in those who were resected. Two patients had evidence of systemic disease in addition to CNS spread. Three women were BRCA1/2 Positive. Following initial radiotherapy, one patient received adjuvant chemotherapy followed by olaparib maintenance, one received 13 cycles of bevacizumab/olaparib, followed by olaparib maintenance. A third patient was treated with olaparib/bevacizumab and two patients received olaparib monotherapy, both of whom continued on therapy. All received olaparib therapy during their treatment and all had minor dose modifications due to side effects. Mean survival from initial cancer diagnosis was 62.4 ± 20.4 months. Mean duration of PARPi therapy was 27.6 ± 16.8 months. Mean survival following CNS recurrence was 22.8 ± 12 months. One patient is disease-free, two patients are alive with stable disease, one patient is alive but off treatment secondary to progression, and one patient is deceased secondary to progression of her brain metastases after being on PARP therapy for 18 months. The cohort remained highly functional across the trajectory of their disease with ECOG scores of 1 (n=4) or 0 (n=1). The results of this single institution retro-

spective evaluation suggest olaparib in combination with radiotherapy +/- bevacizumab is well tolerated and can provide additional benefit in patients with brain metastases secondary to ovarian carcinoma.

MULTIMODALITY

MLTI-01. STUDY ON THE ASSOCIATION BETWEEN PRONE LOCATIONS AND PROGNOSIS OF BREAST CANCER BRAIN METASTASES VIA VOXEL ANALYSIS

Hairong Wang[1], Hao Duan[1], Hongyu Chen[1], Dongping Jiang[1], Yonggao Mou[1], Maojin Yao[2], Chengcheng Guo[1]; [1]Sun Yat-sen University Cancer Center, Guangzhou, China, [2]Guangzhou Medical University, Guangzhou, China

PURPOSE: This study aimed to analyze the preferred locations of secondary brain tumors of breast carcinoma according to different biological characteristics. METHOD: 161 Breast cancer brain metastasis (BCBM) patients diagnosed between January 2007 and February 2018 were retrospectively analyzed. MR images when brain metastases occurred were collected, registered, segmented. The frequency and p-value heatmaps were constructed to compare two biological phenotypes using two-tailed Fisher's exact test. Age, treatments, the status of ER, PR, and HER2, luminal subtype, tumor marker levels in peripheral blood including CEA, CA19-9, and CA15-3 were statistically analyzed. Survival data were analyzed by Kaplan–Meier method, log-rank test, and multivariate logistic regression. RESULT: The frequency heat map shows lesions of patients with BCBM are more inclined to the cerebellar hemisphere. Older patients(>49 years old, median age) mainly occur in the left frontal lobe, the right parietal lobe, and adjacent meninges comparing with white matter of the left parietal lobe, cerebellar vermis, and areas around the fourth ventricle among younger patients and the difference is significant. Patients with tumors located on the surface of the brain are more likely to undergo surgical treatment, however, conservative treatment was considered if metastases are located at the midline structure. ER and PR-positive and HER-2 enriched patients have more significance in metastases, at the left parieto-occipital junction area, frontal lobe, parietal lobe, cerebellar hemisphere, and adjacent meninges. Metastases with high levels of CEA are found significantly at areas around the central anterior gyrus. Lesions with an elevated level of CA19-9 and CA15-3 tend to be frontal, parietal, and occipital. Besides, HER-2 enriched in primary sites and a normal level of CA15-3 in peripheral blood were two independent protective factors in determining prognostic outcomes. CONCLUSION: The preferred locations of BCBM could be clues of further study and helpful for clinical strategies.

MLTI-02. IMPACT OF DRIVER MUTATIONS ON TIMING, PATTERN, TREATMENT, AND OUTCOME IN PATIENTS WITH BRAIN METASTASES FROM NON-SMALL CELL LUNG CANCER

Stephanie Jünger, Marie-Lisa Eich, Anna-Katharina Meissner, Maximilian Ruge, Roland Goldbrunner, Stefan Grau; University of Cologne, Cologne/NRW, Germany

OBJECTIVE: To assess the impact of driver mutations in non-small cell lung cancer (NSCLC) on the formation and treatment outcome of brain metastases (BM). PATIENTS AND METHODS: We retrospectively analyzed patients with BM from NSCLC with respect to driver mutations and assessed timing and pattern of BM development as well as local cerebral control and survival after BM treatment. RESULTS: We included 253 patients. Histology was adenocarcinoma in 223, squamous cell carcinoma in 25 and not otherwise specified (NOS) in five patients. All tumors were analyzed for known alterations in NSCLC by panel sequencing and fluorescence in situ hybridization (FISH). An activating *KRAS* mutation (n=85) was the most prevalent mutation, followed by activating EGFR mutation (n=31) and *MET* amplification (n=29). Other mutations were detected in 27 patients. No alterations were found in 102 patients. Time to BM development did not differ between the molecular groups (p=.22), nor did the number (p=.72) or location (supra- vs. infratentorial; p=.76) of the BM. Patients underwent multimodal cerebral treatment comprising surgery followed by radiotherapy and/or stereotactic radiosurgery (n=138), whole brain radiotherapy (n=13) or stereotactic radiosurgery alone (n=102). Systemic treatment was initiated or continued after BM therapy in 169 patients and its frequency did not differ significantly between genotypes (p=.08) while the modality of medical treatment depended on genotype (p<0.0001). The latter showed longer local cerebral control rates compared to other mutations (0.23) and a longer overall survival compared to *KRAS* and wild type genotypes (p=.015). Systemic treatment (HR 2.1 95%CI 1.4–3.0; p<.0001) and a good clinical status (HR 2.1 95%CI 1.2–3.7; p=0.014) were the only independent factors for further survival. CONCLUSION: The actual known driver mutations do not influence BM formation. Specific genotypes show a better oncological course, presumably due to available molecular treatment.

MLTI-03. THE RELEVANCE OF THE COUNT OF BRAIN METASTASES FOR TREATMENT AND OUTCOME IN NSCLC

David Reinecke[1], Stephanie T. Jünger[1], Martin Kocher[2], Maximilian Ruge[2], Daniel Ruess[2], Roland Goldbrunner[1], Stefan J. Grau[1]; [1]Center for Neurosurgery, Department of General Neurosurgery, Faculty of Medicine and University Hospital Cologne, University of Cologne, Cologne/NRW, Germany, [2]Center for Neurosurgery, Department of Stereotaxy and Functional Neurosurgery, Faculty of Medicine and University Hospital Cologne, University of Cologne, Cologne/NRW, Germany

BACKGROUND AND PURPOSE: While data reporting the number of brain metastasis as a prognostic factor for patients with NSCLC, we analyzed whether the prognostic importance of the mere count of brain metastasis in a modern, multimodal treatment setting. PATIENTS AND METHODS: We retrospectively analyzed patients treated for BM from non-small lung cancer between 2010 and 2020. Demographics, baseline characteristics, and tumor-associated parameters were retrieved from an electronic database. Prognostic factors for local cerebral control and survival were identified using the log-rank test and Cox regression analysis. RESULTS: We included 343 consecutive patients (male n=187, female n=156; median age 61 years). Histological subtypes were adenocarcinoma (n=283), squamous-cell carcinoma (n=42) and neuroendocrine carcinoma (n=18). The median number of BM was one (range 1–20). Single (n = 189), oligo (n=110) and multiple BM (n=44) showed in total a median follow up of 10 months (minimum 1, maximum 142). Treatment comprised surgical resection (n=218) with radiotherapy, stereotactic radiosurgery (n=125) and adjuvant systemic therapy (n=203). The median local cerebral control was 11 months (95%CI 8.5 – 13.5) and the median overall survival was 16 months (95%CI 12.8 – 19.2). The number of BM did not influence local control and overall survival rates (p = 0.234 and p = 0.210, respectively). Controlled systemic disease (HR 0.42; 95% CI 0.2284–0.633; p<0.0001), clinical status (Karnofsky Performance Score > 70; HR 0.41; 95% CI 0.265–0.661; p<0.0001) and adjuvant systemic therapy (HR 0.38; 95% CI 0.279–0.530; p<0.0001) were independent prognostic factors for survival. CONCLUSIONS: The mere number of brain metastases is not a prognostic factor for survival and local cerebral control in a multimodal treatment setting.

MLTI-04. THE ROLE OF THE OUTPATIENT REGISTERED NURSE IN THE CARE OF BRAIN METASTASES

Juliana Hernandez, Amanda Lavarco, Kurt David; Memorial Sloan-Kettering, New York, NY, USA

INTRODUCTION: Brain metastases is a complex disease, requiring a skilled clinical team to deliver medical and surgical care. The nurse is an integral member of the interdisciplinary team. Despite this, the role of the nurse in brain metastasis care has been neglected in the literature. Moreover, while education for neurology nursing exists, there is a paucity of literature defining the nursing care specific to brain metastases. The aim of this study was to describe the essential nursing functions in brain metastases within medical and surgical clinics. METHODS: A working-group comprised of 2 registered nurses and a clinical nurse specialist in specialty brain metastases at Memorial Sloan-Kettering Cancer Center was formed. A KSA framework was used to develop a survey to assess nurses' knowledge, skills, and attitudes regarding care of patients with brain metastases. 2 nurses were surveyed. Oncology nursing competencies were scored by medicine and surgical nurses for importance. Mean scores were calculated and ranked. RESULTS: Nurses consistently reported care coordination; symptom management and monitoring parameters; knowledge of treatment modalities; and referrals as key competencies. More variably endorsed competencies included access devices (implanted port and Omaya); managing immunocompromised patients; and legal issues (consent). The nurses reported important knowledge includes screening and treatment guidelines; epidemiology; disease states including brain metastases and leptomeningeal disease; and tumor histology. Important skills include neurological exam; triage; critical thinking; and patient education. Important attitudes include being empathetic, communicative, positive, truthful, and realistic. CONCLUSION: As the care of the patient with brain metastases evolves, interdisciplinary clinical practice models with advanced nursing training must occur. As the repertoire of clinical trials for patients with brain metastases continues to expand, future studies should assess the effects of specialized nursing training on clinical outcomes in patients with brain metastases.

MLTI-05. ADJUVANT RE-IRRADIATION IMPROVES LOCAL CONTROL OF SURGICALLY RESECTED RECURRENT BRAIN METASTASES

Jessica Wilcox[1], Samantha Brown[1], Anne Reiner[1], Robert Young[1], Justin Chen[2], Tejus Bale[1], Marc Rosenblum[1], William Newman[3], Cameron Brennan[1], Viviane Tabar[1], Kathryn Beal[1], Katherine Panageas[1], Nelson Moss[1]; [1]Memorial Sloan Kettering Cancer Center, New York, NY, USA, [2]Joan and Sanford I. Weill Medical College of Cornell University,