Abstracts

P16 LEPTOMENINGEAL DISEASE

P16.01.A. FACTORS PREDICTING COGNITIVE IMPAIRMENT AFTER INTRATHecal METHOTREXATE TREATMENT IN PATIENTS WITH NON-SMALL CELL LUNG CANCER AND LEPTOMENINGEAL DISEASE


BACKGROUND: Leptomeningeal disease (LD) is a devastating cancer-related neurological complication, LD accounts for 4-15% of patients with non-small cell lung cancer (NSCLC). In this population, the median overall survival (OS) with intrathecal (IT) methotrexate (MTX) plus systemic therapy (ST) is 4-6 months. Until now, disease and treatment-related cognitive impairment (CI) has been poorly studied in this group. MATERIAL AND METHODS: Patients with NSCLC and LD treated with IT MTX in our institution between 2010 and 2021 were retrospectively studied. LD was diagnosed based on positive cerebrospinal fluid cytology or radiological findings in the brain/spinal MRI plus suitable clinical signs/symptoms. IT MTX (12mg twice weekly for 4 weeks, then 12mg weekly for 5 weeks) was given in combination with ST. Patients with cognitive characteristics and patient-reported CI were assessed at baseline and at 3-months post IT MTX. A Kaplan-Meier survival analysis was performed. Primary endpoint: predictive factors of CI at 3m post IT MTX. Secondary endpoint: prognostic factors. RESULTS: Out of 55 patients included, 51% were male and median age at LD diagnosis was 59 years old (range 38-78). Most patients had an ECOG PS1 (76.4%) and adenocarcinoma histology (83.6%). 47% of patients harbored EGFR mutation. In 23.6% of patients LD was diagnosed synchronously with lung tumor and in 76.4% of patients LD was diagnosed with lung tumor recurrence. The median time to LD development was 8m (range 0-73). Clinical features at LD diagnosis were 43.7% infratentorial symptoms, 29% CI, 20% multiple symptoms and 7% asymptomatic. At LD diagnosis, 53% of patients had synchronous brain metastases (BM) and in 38% the systemic disease was not controlled. 85.5% of patients received ST concurrently with IT MTX (N=22 chemotherapy, N=22 TKIs and N=3 immunotherapy). 14.5% of patients did not receive ST.

Median OS from IT was 5m (95% CI 1.3-8.6). ECOG PS and ST administered concurrently with IT MTX was associated with longer OS (p<0.05). 23.6% of patients developed CI at 3m post IT therapy. Median OS for patients without and with CI post IT therapy was 6m (95% CI 0.7-11.3) vs 4m (95% CI 0.3-5.7) (p=0.15). Patients with CI showed higher ECOG PS at baseline (score2±2m; the percentiventricular Fazekas’ score) (p=0.033), women (p=0.01) and those 60 years (p=0.04) were more likely to present CI 3m post IT MTX. The presence of cardiovascular risk factors, previous brain irradiation at BM and concurrent CI was not statistically associated with CI. CONCLUSION: In this cohort, 24% of patients with NSCLC and LD treated with IT MTX will develop CI 3m post treatment. Baseline leukoen cephalopathy, female gender, older than 60 years old were more likely to exhibit CI after IT MTX. A better characterization of these patients is warranted to develop new treatment strategies to prevent/reduce CI.

P16.02.B. LEPTOMENINGEAL DISSEMINATION IN GLIOMAS IN NATIONAL RESEARCH INSTITUTE OF ONCOLOGY IN GLIWICE EXPERIENCE

E. Nowicka, H. Grzbiela, K. Widera, Ł. Zarudzki, A. Grzadziel, R. Tarnawski; MSC National Research Institute of Oncology, Glawice, Poland.

BACKGROUND: The leptomeningeal dissemination (LMD) in the course of gliomas is rare. According to literature it can affect 4.7% of all patients with gliomas. LMD can be diagnosed at the initial clinical or imaging stage but also late in the course of the disease. The time of recurrence. The standard therapy has not yet been determined. We aimed to present the clinical features and prognosis in retrospective analysis of patients with LMD in gliomas in National Institute of Oncology in Glawice, Poland. MATERIAL AND METHODS: Thirty-four patients with leptomeningeal dissemination in course of treatment of brain gliomas were identified. There were 16 men and 4 women. Median age of pts was 35.5 y (range 18-51). All tumours were supratentorial at diagnosis. There were 6 glioblastomas, 3 oligodendrogliomas and 11 glioblastomas. In two patients LMD was found at initial diagnosis of GBM. The majority of patients (15 pts) presented clinical symptoms and in 5 asymptomatic pts LMD was diagnosed in MRI. The diagnosis was confirmed in cranial
MRI. One patient was operated due to rapid clinical progression of spinal compression symptoms. All but one patient were offered palliative therapy. Radiotherapy was prescribed to 16 patients: in 7 pts for whole brain to C2, in 3 pts for cisternal space, in 2 pts local therapy was performed. Mean dose of RT was 28.7 Gy (range 18-45 Gy/g). In 8 patients radiotherapy was combined with chemotherapy and chemotherapy as sole treatment was prescribed to 2 pts (Lomu, EP). RESULTS: Mean time from initial diagnosis to LMD diagnosis was 46 mo (range 0.4-195 mo) for all patients and for non-GBM and GBM patients were 81.4 mo (16-199 mo) and 14.0 mo (0.4-27 mo) respectively. In 7 patients LMD was diagnosed concurrently with local relapse. In remaining mean time from local relapse to LMD was 4.6 mo (1.2-20.0 mo). Mean OS duration was 8 mo (0.4-37 mo). The palliative effect as improvement in clinical symptoms was achieved in 13 pts. CONCLUSION: LMD in gliomas is rare but should be kept in mind while clinical symptoms in glioma patients occur. The prognosis of LMD is poor. Radiotherapy has palliative intent and it can affect the clinical symptoms and survival.

P16.03.A. EPITHELIOID GLIOBLASTOMA REQUIRES RAPID TREATMENT AND BRAF INHIBITORS SHOULD BE MADE READILY AVAILABLE FOR THEIR TREATMENT
V. Hurwitz,1 J. Lavrador1, K. Chia1, A. Swapnall1, O. Al-Salihi1, R. Bhangoo1, F. Vergani1, K. Ashkan1, S. Hedges1, E. Kostik1, A. Suarez2, C. Robinson1; Kings College Hospital, London, United Kingdom, 4Guy’s and St Thomas, London, United Kingdom.

BACKGROUND: Epithelioid glioblastoma is a rare subtype of glioblastoma. We examine two cases who presented acutely with symptoms of headache, neck stiffness and an eye spasm. The purpose of this case report is to describe their management, the spread of tumour disease and predict the ability of RAF inhibitors agents be made readily available for this subtype.

MATERIAL AND METHODS: The clinical records including pathology and surgical reports, multi-disciplinary team meeting documents, oncology plan and patient notes have all been reviewed alongside the literature on epithelioid GBM and BRAF V600e mutations and inhibitors. RESULTS: Patients were females aged 25 and 32 presenting with acute onset headache and neck stiffness to emergency Department. The 25 year old had developed a new lesion within seven days of the onset symptoms, her tumour was right frontal with midline shift. The 32 year old had symptoms for 10 days prior to presentation, the tumour was right temporal. They both underwent craniotomies. The frontal tumour was totally resected, while the temporal lobe tumour was haemorrhagic in nature and minimally debulked. Pre-operative stealth imaging showed that there had been an increase in the size of the temporal lesion in the fourteen days since presentation. Histology proved these to be epithelioid GBM’s with BRAF V600e mutations, IDH wild-type and TERT promoter mutant. Full pathology reports were available within one week. The frontal patient began chemo-radiation sixteen days from her surgical date. On day two she was admitted with severe headache and nausea. She became agitated, confused, and transferred back to the neurosurgery unit for management of hydrocephalus. LMD was diagnosed and simultaneously treated for this and hydrocephalus. Clinically she suffered storming, passing away exactly eight weeks from presentation. Seven days after surgery the temporal lobe tumour patient suffered a seizure and admitted for symptom management and expedite oncology treatment. She passed away six days under palliative care. CONCLUSION: The prognosis for epithelioid Glioblastoma is limited to weeks to short months. Extent of resection in this case studies demonstrates benefit in delaying progression though it is clear that time is of the essence from presentation, to surgery, to adjuvant treatment. Neither of these tumours were methyalted meaning the standard treatment for glioblastoma is likely to lack efficacy; BRAF inhibitors should be made readily available for this rare subtype to commence treatment expeditiously. Both patients suffered distressing neurological symptoms in their final days which require expert management and are best managed in a neurosurgical centre.

P16.04.B. PALLIATIVE CSF DIVERSION IN SYMPTOMATIC LEPTOMENINGLE MALIGNE METASTASES: A FEASIBILITY ANALYSIS OF RISKS AND BENEFITS
O.T. Alhalabi, A. W. Unterberg, A. Younis; Department of Neurosurgery, Heidelberg University Hospital, Heidelberg, Germany.

BACKGROUND: Leptomeningeal metastases (LM) represents a terminal condition in a subset of patients with primary extra-cranial malignancies. With improved survival rates under novel systemic therapies for extra-cranial primary tumours, the role of cerebrospinal fluid (CSF) diversion via ventriculo-peritoneal shunts (VP-shunt) for symptom control of hydrocephalic LM is becoming increasingly important. This study hence aimed to describe this patient cohort and weigh out benefits against adverse events of palliative VP-shunt placement.

MATERIAL AND METHODS: A single-center retrospective analysis of all consecutive adult patients with VP-shunt placement over a period of six years was performed. The study period was from January 1st 2012 to December 31st 2017. VP-Shunt placement was performed for patients with a median age of 53 (18-78) years (13 males, 25 females) under VP-Shunt placement. The most common underlying oncological conditions were breast cancer (n=21, 55%) and non-small cell lung cancer (NSCLC, n=11, 29%). Two patients received systemic therapy for their primary disease. RESULTS: 38 patients with a median age of 53 (18-78) years (13 males, 25 females) underwent VP-Shunt placement. The most common underlying oncological conditions were breast cancer (n=21, 55%) and non-small cell lung cancer (NSCLC, n=11, 29%). Median survival from shunting was 2.1 months (95% CI 0.5 to 3 months). CONCLUSION: VP-shunt placement could relieve symptoms of intracranial hypertension secondary to LM of primary solid tumours without a higher risk of shunt complications compared to non-oncological patients, with many LM patients pursuing further oncologic therapy. However, decision-making regarding VP-shunt placement in LM patients still remains a palliative nature.

P17.01A. RERADIATION BY GLOSSOBASTOMA RECURRENT WITH VMAT TECHNIQUE
M. Theodorou1, I. Polyarpour1; 1Bank of Cyprus Oncology Center, Nikosia, Cyprus, 2European University Cyprus, Nikosia, Cyprus.

BACKGROUND: Patients who have been treated with reirradiation for recurrent glioma reported survival benefits.

This study aims to investigate whether re-irradiation of recurrent glioma with 45 Gy dose can increase the overall survival of patients. MATERIAL AND METHODS: A retrospective analysis of 35 patients re-irradiated for high-grade glioma recurrence between 2012 and 2020 was performed. All included patients met the following criteria: a) histopathological confirmation of primary brain cancer at initial diagnosis; b) a history of initial primary radiation; c) histological and/or imaging modality confirmation of recurrence. Outcome metrics included overall survival, prognostic factors for survival, and treatment-related toxicity. RESULTS: After the end of re-irradiation the median overall survival was 11 months (95% confidence interval, 7-14 months). From the patients evaluated in the current study after the end of re-irradiation the progression free survival was 6 months (3.8 - 8 months) while after the end of first radiation was 13 months (8 - 17.9 months). Our findings suggest that re-irradiation might prolong survival rates. CONCLUSION: Recurrent Glioblastoma WHO IV is associated with a median overall survival of less than a year and the majority of patients have profound tumor-related symptoms. The results of this study suggest that re-irradiation may prolong the overall survival.

P17.02.A. IPAX-I: PHASE 1/2 STUDY OF 131I-IODOPHENYLALANINE (131I-IPPA) COMBINED WITH EXTERNAL RADIATION THERAPY AS TREATMENT FOR PATIENTS WITH RELAPSED GLOSSOBASTOMA
J. Neubauer1, A. Lehetseder1, E. Nollmüller1, T. Traub-Wiedinger1, F. Fritz1, H. Genn1, J. Feichtinger1, T. Brown4, C. Hayward6, KIEPER UNIERSITÄTSKLINIKUM NEUMÜDLOS Campus, Division of Internal Medicine and Neurooncology, Linz, Austria, 2Medical University of Vienna, Division of Nuclear Medicine, Vienna, Austria, 3Örskenskindl Linz Barmherzig Schwestern, Department of Nuclear Medicine and Endocrinology, Linz, Austria, 4Örskenskindl Linz Barmherzig Schwestern, Division of Radiooncology, Linz, Austria, 5Telfix Pharmaceuticals Limited, Melbourne, Australia.

BACKGROUND: A novel therapeutic approach using molecularly targeted radiation is currently in development for patients with recurrent GBM. Most GBM, however, overexpress the low affinity trans- porter 1 (LAT-1), which is able to internalize the small-molecule amino acid derivative, 4-L-[131I]iodophenylalanine (131I-IPPA). In preclinical research, combining 131I-IPPA with external radiation therapy (XRT) yielded addi-