RESULTS: A total 105 patients were identified. 84 patients underwent biopsy and 21 patients underwent surgical resection. Their median age were 63 [31–78] and 68 [44–77], respectively. Their Karnofsky Performance Status (KPS) were 70 [30–100] and 70 [40–100]. There were any significant difference. Patients undergoing biopsy and those undergoing resection had comparable rates of complications for all complication type. Overall, 4 biopsy patients and 5 resection patients experienced at least one complication. They were composed of 2 asymptomatic bleeding, 1 wound abscess, 1 hydrocephalus in biopsy patients, 1 epidural abscess, 1 epilepsy, 1 chronic subdural hematoma, 2 temporary hemiparesis. Although the days from surgery to chemotherapy were significantly shorter in patients underwent biopsy than in those underwent resection (P=0.0015), PFS was significantly longer in patients underwent resection than in those underwent biopsy (P=0.0403), whereas there was no difference in OS.

DISCUSSION: Resection could delay the postoperative treatment. In this study, there was a significant delay of postoperative treatment in resection patients, however, CR/CRu rate after MTX was significantly better in those underwent resection than biopsy. We can see that resection for PCNSL might not necessarily worsen the prognosis.

ML-05

ONE-YEAR FOLLOW-UP DATA OF PHASE I/II STUDY OF TIRABRUTINIB IN PATIENTS WITH RELAPSED OR REFRACTORY PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA

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In March 2020, Tirabrutinib (TIR), a second-generation oral Bruton's tyrosine kinase inhibitor, was approved for the indication of relapsed or refractory PCNSL (r/rPCNSL) based on the results of a phase I/II study in Japan. In this study, 44 Japanese patients with r/rPCNSL were treated with TIR QD at 320 mg, 480 mg, or 480 mg in the fasted condition (480 mg fasted QD). The primary endpoint was overall response rate (ORR) assessed by an independent review committee according to International PCNSL Collaborative Group criteria. We previously reported the results of this study with data cutoff in June 2019 (Narita et al. Neuro Oncol. 2020). In the report, 17 of 44 patients were treated with TIR at 480 mg fasted QD which is an approved dose, and had ORR of 52.9%, median progression-free survival of 5.8 months, and median overall survival of not reached (median follow-up: 3.8 months). In 44 patients, ORR was similar among patients harboring either of the oncogenic mutants *CARD11*, *MYD88*, *CD79B*, or wild type. Throughout the whole patients, most common adverse events (AEs) at any grade were rash (31.8%), neutropenia (22.7%), leukopenia (18.2%), and lymphopenia (15.9%), and grade ≥3 AEs were neutropenia (9.1%), lymphopenia, leukopenia, and erythema multiforme (6.8% each). One patient with 480 mg QD had grade 5 AEs (pneumocystis jirovecii pneumonia and interstitial lung disease). We will present one-year follow-up data of this study at the meeting. As of data cutoff (February 2020), 11 of 44 patients continued to receive TIR, including 6 patients with 480 mg fasted QD. Updated data for overall survival, duration of response, and time to onset of AEs will also be presented. TIR is a promising new treatment for r/rPCNSL.

ML-06

DIAGNOSTIC VALUE OF LIQUID BIOPSY FOR CNS LYMPHOMA BY DETECTION OF SPECIFIC GENE MUTATIONS IN THE CEREBROSPINAL FLUID

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BACKGROUNDS & PURPOSE: Central nervous system lymphoma (CNSL) is the second most common primary malignant brain tumor. Brain biopsy is indispensable to confirm the diagnosis of CNSL, but has a potential risk of inducing hemorrhagic complications in the brain. Therefore, liquid biopsy using the cerebrospinal fluid (CSF) has attracted an attention as a less invasive diagnostic method. In this study, we established a digital PCR-based method to detect *MYD88* mutations in CSF and evaluated its efficacy. METHODS: Matched CSF and biopsy samples from CNSL patients collected before the start of chemotherapy were used. Cellular DNA and cell free DNA (cfDNA) of CSF were separately extracted from the pellet and the supernatant fraction of CSF, respectively. Presence of the *MYD88* L265P mutation was examined in each fraction by the digital PCR. The mutational status obtained by liquid biopsy was compared with that of the matched biopsy specimen examined by pyrosequencing. RESULT: A total of 36 paired samples were used. When the cutoff value of Target/Total ratio was 0.25%, sensitivity, specificity, and area under the curve (AUC) of the digital PCR detection using cellular DNA were 92.9%, 100%, and 0.95, respectively, while they were 100%, 100%, and 1.00 using cfDNA. CONCLUSION: We showed that the digital PCR method was highly sensitive and specific in detecting *MYD88* mutations in the CSF. We propose that CSF liquid biopsy may serve a clinically applicable surrogate to make a diagnosis of CNSL.

ML-07

HIGH EXPRESSION OF PD-L1 ON TUMOR-ASSOCIATED MACROPHAGE IS A PREDICTIVE FACTOR FOR FAVORABLE PROGNOSIS IN PCNSL

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PD-L1 and PD-L2 expression on tumor cells and tumor-infiltrating immune cells in primary central nervous system lymphoma (PCNSL) remains unclear. In the present study, we investigated the expressions of PD-L1 and PD-L2 in surgical specimens from needle biopsies and craniotomies to compare tumor tissue with surrounding tumor tissue (peritumoral tissue) and analyzed the correlation between expression of PD-L1/PD-L2 and survival in patients with PCNSL. We retrospectively analyzed the cases of 70 patients histologically diagnosed with PCNSL (diffuse large B-cell lymphoma). Immunohistochemistry for CD20, CD68, PD-L1, and PD-L2 was performed. In cases with specimens taken by craniotomy, the percentages of PD-L1- and PD-L2-positive macrophages were evaluated in both tumor and peritumoral tissue. The Kaplan-Meier method with log-rank test and Cox proportional hazard model were used for survival analysis. The tumor cells did not express very much PD-L1 and PD-L2, but macrophages expressed PD-L1 and PD-L2 in most of the patients. The median percentage of PD-L2-positive cells was significantly higher among peritumoral macrophages (32.5%; 95%CI: 0–94.6) than intratumoral macrophages (27.5%; 95%CI: 0–81.1, p=0.0014). There was a significant correlation between the percentages of PD-L2-positive intratumoral macrophages and PD-L2-positive peritumoral macrophages (p=0.0429), with very low coefficient correlation (ρ=0.098535). PD-L1 expression on macrophages was significantly associated with biological factors (intratumoral macrophages: better KPS, p=0.0008; better MSKCC score, p=0.0103; peritumoral macrophages: low proportion of LDH elevation, p=0.0064) and longer OS (for intratumoral macrophages: high PD-L1=60 months, 95%CI=30–132.6; low PD-L1=24 months, 95%CI=11–48; p=0.032; for peritumoral macrophages: high PD-L1=60 months, 95%CI=30.7-NR; low PD-L1=14 months, 95%CI=3–26). PD-L1 expression on peritumoral macrophages was strongly predictive of a favorable outcome (HR=0.30, 95%CI=0.12–0.77, p=0.0129). Macrophages in intratumoral and peritumoral tissue expressed PD-L1 and PD-L2 at a higher rate than tumor cells. PD-L1 expression, especially on peritumoral macrophages, seems to be an important prognostic factor in PCNSL.

ML-08

SAFETY AND EFFICACY OF CONSOLIDATION CYTARABINE FOR NEWLY-DIAGNOSED PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA

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BACKGROUNDS: While consolidation therapies which incorporate whole brain radiotherapy (WBRT) and/ or chemotherapies such as high dose (HD)-cytarabine are commonly applied following induction chemotherapies in primary central nervous system lymphoma (PCNSL), the optimal treatment for consolidation therapy has not been established. We aimed to investigate the safety and efficacy of consolidation cytarabine with a dose modification policy in PCNSL. Patients and METHODS: PCNSL patients initially treated by R-MPV (rituximab, methotrexate, procarbazine and vincristine) and subsequently treated either by WBRT of 24Gy followed by cytarabine (WBRT-AraC group), or cytarabine alone (AraC group) were identified. WBRT was deferred in patients 71 years old or younger who had obtained a complete response (CR) after R-MPV. Cytarabine was dose-modified according to age groups (3 g/m2 in patients 70 years old or younger, 2 g/m2 in patients aged 71–75 years, 1 g/m2 in patients aged 76–80 years). Toxicity profiles, progression-free survival (PFS), overall survival (OS) were analyzed. RESULTS: Twenty-five patients were identified (median age: 69 [range: 34–80], median KPS:70 [range: 40–90]), including 11 patients from the WBRT-AraC group, and 14 patients from the AraC group. Median PFS was unreached in the WBRT-AraC group, and 41.8 months in the AraC group. Median OS was unreached in both groups. The overall rate of grade 3/4 hematologic