the course of LE, and to investigate its impact on long-term neurocognitive and behavioural outcome. METHODS: A French retrospective, multicenter study including 35 children under 5 years of age, treated between 2009 and 2017, with a median follow up of 72 months. All follow-up MRIs including assessment of the severity of the LE (Fazekas and CTCAE grading) and all NP evaluations were centrally rewieved. RESULTS: 25/34 evaluable patients presented a LE during follow up, in a median delay of 2 months (1 - 17 months) after the start of chemotherapy. Grade 2 and 3 abnormalities were correlated with higher cumulative dose of ITV -MTX (p=0,01). Full Scale IQ (FSIQ) and Wechsler indexes were in the average or low average of the reference population. FSIQ was deficient in 7/20 evaluable patients. Processing speed (PSI) was the most frequently impaired neurocognitive domain: 9/20 patients with borderline or very low score, all having received a significantly higher cumulative dose of ITV-MTX (p=0,04). A decrease in overall NP scores was observed in patients for whom grade 2 or 3 LE persisted at the end of follow-up with an average FSIQ estimated at 82.1 (SD 16.9) versus 94.2 (SD 20.6). This decrease was significant for PSI (p=0,049). LE and neurocognitive impairments were not correlated with a younger age at diagnosis. CONCLUSION: This study confirmed the responsibility of MTX, and in particular ITV-MTX therapy in the onset and, most often, persistence of LE and its association with neurocognitive disorders.

MEDB-14. CLINICAL OUTCOME OF PEDIATRIC MEDULLOBLASTOMA PATIENTS WITH LI-FRAUMENI SYNDROME

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PURPOSE: The prognosis for SHH-medulloblastoma (MB) patients with Li-Fraumeni syndrome (LFS) is poor. Due to lack of comprehensive data for these patients, it is challenging to establish effective therapeutic recommendations. We here describe the largest retrospective cohort of pediatric LFS SHH-MB patients to date and their clinical outcomes. PATIENTS AND METHODS: N=31 patients with LFS SHH-MB were included in this retrospective multicenter study. *TP53* variant type, clinical parameters including treatment modalities, event-free survival (EFS) and overall survival (OS), as well as recurrence patterns and incidence of secondary neoplasms, were evaluated. RESULTS: All LFS-MBs were classified as SHH subgroup, in 30/31 cases based on DNA methylation analysis. The majority of constitutional *TP53* variants (72%) represented missense variants, and all except two truncating variants were located within the DNA-binding domain. 54% were large cell anaplastic, 69% gross totally resected and 81% had M0 status. The 2-(y)ear and 5-(y)ear EFS were 26% and 8,8%, respectively, and 2y- and 5y-OS 40% and 12%. Patients who received post-operative radiotherapy (RT) followed by chemotherapy (CT) showed significantly better outcomes (2y-EFS:43%) compared to patients who received CT before RT (30%) ($p<0.05$). The 2y-EFS and 2y-OS were similar when treated with protocols including high-dose chemotherapy (EFS:22%, OS:44%) compared to patients treated with maintenance-type chemotherapy (EFS:31%, OS:45%). Recurrence occurred in 73.3% of cases independent of resection or M-status, typically within the radiation field (75% of RT-treated patients). Secondary malignancies developed in 12.5% and were cause of death in all affected patients. CONCLUSIONS: Patients with LFS-MBs have a dismal prognosis. This retrospective study suggests that upfront RT may increase EFS, while intensive therapeutic approaches including high-dose chemotherapy did not translate into increased survival of this patient group. To improve outcomes of LFS-MB patients, prospective collection of clinical data and development of treatment guidelines are required.

MEDB-15. DYNAMIC CHROMATIN ALTERATION INDUCES ONCOGENIC HIJACKING BY ESSENTIAL TRANSCRIPTIONAL FACTORS DURING SHH MEDULLOBLASTOMA TUMORIGENESIS

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Medulloblastoma is a malignant brain tumor that occurs in the cerebellum, most frequently in children. Medulloblastoma is molecularly classified into four major groups, and therapies are now being developed according to the nature of these groups and subgroups. However, there are currently no effective molecularly targeted drugs for most of these groups. In recent years, we have been analyzing the genomes of medulloblastomas to identify genetic mutations involved in tumorigen-