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Clinical outcome of pediatric medulloblastoma patients with Li-Fraumeni syndrome

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Abstract

Background: The prognosis for Li-Fraumeni syndrome (LFS) patients with medulloblastoma (MB) is poor. Comprehensive clinical data for this patient group is lacking, challenging the development of novel therapeutic strategies. Here, we present clinical and molecular data on a retrospective cohort of pediatric LFS MB patients.

Methods: In this multinational, multicenter retrospective cohort study, LFS patients under 21 years with MB and class 5 or class 4 constitutional TP53 variants were included. TP53 mutation status, methylation subgroup, treatment, progression free- (PFS) and overall survival (OS), recurrence patterns, and incidence of subsequent neoplasms were evaluated.

Results: The study evaluated 47 LFS individuals diagnosed with MB, mainly classified as DNA methylation subgroup "SHH_3" (86%). The majority (74%) of constitutional TP53 variants represented missense variants. The 2- and 5-year (y-) PFS were 36% and 20%, and 2- and 5y-OS were 53% and 23%, respectively. Patients who received post-operative radiotherapy (RT) (2y-PFS: 44%, 2y-OS: 60%) or chemotherapy before RT (2y-PFS: 32%, 2y-OS: 48%) had significantly better clinical outcome then patients who were not treated with RT (2y-PFS: 0%, 2y-OS: 25%). Patients treated according to protocols including high-intensity chemotherapy and patients who received only maintenance-type

chemotherapy showed similar outcomes (2y-PFS: 42% and 35%, 2y-OS: 68% and 53%, respectively).

Conclusions: LFS MB patients have a dismal prognosis. In the presented cohort use of RT significantly increased survival rates, whereas chemotherapy intensity did not influence their clinical outcome. Prospective collection of clinical data and development of novel treatments are required to improve the outcome of LFS MB patients.

Keywords: Li-Fraumeni syndrome; TP53; medulloblastoma; survival.