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MDB-49. OUTCOMES OF SONIC HEDGEHOG (SHH) MEDULLOBLASTOMA (MB) IN CHILDREN AND ADULTS TREATED WITH RISK-ADAPTED THERAPY ON A PROSPECTIVE INTERNATIONAL PROTOCOL. (SJM12)
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BACKGROUND: SJMB12 (NCT01878617) was among the first protocols to treat newly diagnosed MB incorporating molecular subgrouping. METHODS: Tumors were subtyped and TP53 mutation assessed via immunohistochemistry. SHH patients were grouped into 2 strata: S1 (GTR/ NTR; M0) and S2 (residual > 1.5 cm2; MYC/MYCn amplification; M+). Treatment consisted of maximal surgical resection followed by risk adapted craniospinal irradiation (CSI) (S1 = 23.4 Gy CSI; S2 = 36); 54 Gy primary irradiation with proton irradiation. We reported only one case of ototoxicity. CONCLUSION: Of the 660 patients accrued from 2013-2022, 110 were SHH (107 evaluable, 62 in S1 and 45 in S2). Median age was 12.2 yrs. (3.1-39.7) and 67 were males. 98 patients had GTR/NTR, 31 had M+ disease and 63 had nodular desmoplastic histology. TP53 mutation was detected in 7 (11.5%) S1 and 18 (40%) S2. 5-year EFS for S1 and S2 were 84.5 ± 6.4% and 61 ± 11.5%, respectively. Five-year EFS of the S1 was 91.7 ± 5.4% and 28.6 ± 13.9% for TP53 wildtype and TP53 mutant cases, respectively, and 84.2 ± 10.1% and 25.0 ± 21.7% in the S2 cohort. CONCLUSION: Patients with low-risk SHH MB behave very differently. TP53 mutation have excellent survival and may be considered for therapy reduction. TP53 mutation, with or without M+ disease, leads to a dismal outcome that needs novel therapy for cure.