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JOURNAL ARTICLE CORRECTED PROOF

Treatment deintensification in average-risk medulloblastoma: Less is more?

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Extract

Medulloblastoma is a heterogeneous disease in which survival is largely determined by tumor biology and molecular profile. Four molecular variants exist: WNT-activated (WNT), Sonic hedgehog-activated (SHH), and non-WNT/non-SHH Group 3 and Group 4, each further divided into subgroups with distinct molecular features and prognoses.[1] Five-year event-free survival (EFS) is approximately 83% for average-risk medulloblastoma following surgery, craniospinal irradiation (CSI), and adjuvant chemotherapy. Prognosis remains significantly worse, however, for certain molecular groups, including Group 3 and SHH tumors harboring TP53 mutations.[2,3] Outcomes are also poor in infants, who are generally treated with CSI-sparing approaches to reduce long-term morbidity. Survivors experience numerous late effects, including neurocognitive deficits, endocrinopathies, neuropathy, hearing loss, and secondary malignancies. With long survival, the burden of treatment-related toxicities becomes increasingly important. Identifying patients who can safely de-intensify therapy and reduce downstream morbidities without compromising survival and selecting high-risk patients who may benefit from augmented therapy represents a major unmet need.

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