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Risk-stratification for treatment de-intensification in WNT-pathway medulloblastoma: finding the optimal balance between survival and quality of survivorship

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Abstract

Introduction: Advances in molecular biology have led to consensus classification of medulloblastoma into four broad molecular subgroups - wingless (WNT), sonic hedgehog (SHH), Group 3, and Group 4, respectively. Traditionally, children >3 years of age, with no/minimal residual tumor (<1.5 cm^2) and lack of metastasis were classified as average-risk disease with >80% long-term survival. Younger age (<3 years), large residual disease (≥1.5 cm^2), and leptomeningeal metastases either alone or in combination were considered high-risk features yielding much worse 5-year survival (30-60%). This clinico-radiological risk-stratification has been refined by incorporating molecular/genetic information. Contemporary multi-modality management for non-infantile medulloblastoma entails maximal safe resection followed by risk-stratified adjuvant radio(chemo)therapy. Aggressive multi-modality management achieves good survival but is associated with substantial dose-dependent treatment-related toxicity prompting conduct of subgroup-specific prospective clinical trials.

Areas covered: We conducted literature search on PubMed from 1969 till 2023 to identify putative prognostic factors and risk-stratification for medulloblastoma, including molecular subgrouping. Based on previously published data, including our own institutional experience, we discuss molecular risk-stratification focusing on WNT-pathway medulloblastoma to identify candidates suitable for treatment de-intensification to strike the optimal balance between survival and quality of survivorship.

Expert opinion: Prospective clinical trials and emerging biological information should further refine risk-stratification in WNT-pathway medulloblastoma.

Keywords: De-intensification; WNT; medulloblastoma; molecular; risk-stratification; survival.