

Clin Cancer Res. 2023 Jul 27;CCR-23-0348. doi: 10.1158/1078-0432.CCR-23-0348.

Online ahead of print.

A pilot study omitting radiation in the treatment of children with newly diagnosed Wnt-activated medulloblastoma

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PMID: 37498309 DOI: [10.1158/1078-0432.CCR-23-0348](https://doi.org/10.1158/1078-0432.CCR-23-0348)

Abstract

Purpose: Treatment of wingless (WNT)-activated medulloblastoma (WNT+MB) with surgery, irradiation (XRT) and chemotherapy results in excellent outcomes. We studied the efficacy of therapy de-intensification by omitting XRT entirely in children with WNT+MB.

Patients and methods: Tumors were molecularly screened to confirm the diagnosis of WNT+MB. Eligible children were treated within 31 days following surgery with nine cycles of adjuvant chemotherapy per ACNS0331. No XRT was planned. The primary endpoint was the occurrence of relapse, progression, or death in the absence of XRT within the first two years after study enrollment. Four events in the first 10 evaluable patients would result in early study closure.

Results: Fourteen children were prescreened and nine met the protocol definition of WNT+MB. Six of the nine eligible patients consented to protocol therapy and five completed planned protocol therapy. The first two children enrolled relapsed shortly after therapy completion with local and leptomeningeal recurrences. The study was closed early due to safety concerns. Both children are surviving after XRT and additional chemotherapy. A third child relapsed at completion of therapy but died of progressive disease 35 months from diagnosis. Two children finished treatment but immediately received post-treatment XRT to guard against early relapse. The final child's treatment was aborted in favor of a high-dose therapy/stem cell rescue approach. While OS at 5 years is 83%, no child received only planned protocol therapy with all receiving eventual XRT and/or alternative therapy.

Conclusions: Radiation therapy is required to effectively treat children with WNT-altered medulloblastoma.