



Low-stage Medulloblastoma

Thomas RM, Deutsch M, Kepner JL, *et al.*: **Low-stage medulloblastoma: final analysis of trial comparing standard-dose with reduced-dose neuraxis irradiation.** *J Clin Oncol* 2000, 18:3004–3011.

Rating: •Of importance.

Introduction: Medulloblastoma is one of the most frequently diagnosed soft tissue tumors in childhood. The treatment of low-stage medulloblastoma has been controversial, with some studies showing lower doses of radiotherapy are not associated with increased risk of recurrence.

Aims: The primary aim of this study was to evaluate prospectively whether decreasing the radiation dose to the brain and spine would significantly alter relapse-free survival in pediatric patients with low-stage medulloblastoma.

Methods: The Pediatric Oncology Group (POG) and the Children's Cancer Group (CCG) randomized 126 patients with histologically confirmed medulloblastoma of low-stage, as defined by Chang staging and radiographic imaging of brain and spine, with no evidence of cerebrospinal fluid or bone marrow involvement. Patients between the ages of 3 to 21 years all received posterior fossa radiation to a dose of 54 Gy, and were randomized to receive either standard therapy (36 Gy to the neuraxis in 1.8 Gy/d fractions) or reduced therapy (23.4 Gy in 13 1.8 Gy fractions) to the neuraxis. The primary endpoint was to evaluate the event-free survival, as well as isolated neuraxis relapse rate. Of the total number of patients registered for the trial, 81 were evaluable. This is the final analysis of POG8631/CCG923, which was prematurely closed when a planned interim statistical analysis revealed an increased rate of relapse in patients receiving lower-dose radiation therapy.

Results: This final analysis revealed that standard-dose neuraxis radiation therapy had an event-free survival (EFS) of 67% (SE=7.4%) at 5 years. Patients who received reduced-dose neuraxis radiation had an EFS of 52% (SE=7.7%, $P=0.08$). At 8 years, EFS for the standard-dose group was 67%

(SE=8.8%) and 52% (SE=11%) for the reduced-dose group ($P=0.141$). In eligible patients, isolated neuraxis relapse-free survival (as a subset of EFS) was lower among patients who received reduced-dose radiotherapy compared with standard dose treatment ($P=0.015$).

Discussion: With this final analysis of the combined cooperative group trial (POG8631/CCG923), the initial impressions from the interim analysis were confirmed, in that there was an increased risk of early relapse in pediatric patients who received reduced-dose radiotherapy. However, it is now clear with time the differences that were initially observed become much less apparent when examining the 8-year results. Unfortunately, although the study was designed to collect age-stratified neuropsychometric data both before and after therapy, the poor compliance with this part of the study limits any conclusions about the longer-term cognitive effects of each treatment type. Moreover, the high ineligibility rate also limits the interpretation of the results, although the authors did perform both an eligible and registered patient analysis, which were not substantially different.

Editor's comments

The therapy for low-stage medulloblastoma has evolved over the past 10 years, with conflicting data from both cooperative group trials and single-institution pilot studies. This final analysis acts as a benchmark for future studies using radiation therapy, as well as chemotherapy, in the treatment of patients with low-stage disease, both with respect to survival and patterns of recurrence. Although there was a reduction of early neuraxis recurrence with standard-dose radiotherapy, the overall EFS continues to be poor overall in this group of patients. Newer regimens that are devised to utilize either combined-modality and other novel approaches need to be devised in order to further the work reported, with dedication to understanding the effects of treatment on developing nervous system structures in order to better define the risks and benefits of therapy.