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Everolimus for subependymal giant-cell astrocytomas in tuberous sclerosis.

Krueger DA, Care MM, Holland K, Agricola K, Tudor C, Mangeshkar P, Wilson KA, Byars A, Sahnoud T, Franz DN.

Department of Pediatrics, Tuberous Sclerosis Clinic, Cincinnati Children's Hospital Medical Center, Cincinnati, OH 45229, USA.

Abstract

BACKGROUND: Neurosurgical resection is the standard treatment for subependymal giant-cell astrocytomas in patients with the tuberous sclerosis complex. An alternative may be the use of everolimus, which inhibits the mammalian target of rapamycin, a protein regulated by gene products involved in the tuberous sclerosis complex.

METHODS: Patients 3 years of age or older with serial growth of subependymal giant-cell astrocytomas were eligible for this open-label study. The primary efficacy end point was the change in volume of subependymal giant-cell astrocytomas between baseline and 6 months. We gave everolimus orally, at a dose of 3.0 mg per square meter of body-surface area, to achieve a trough concentration of 5 to 15 ng per milliliter.

RESULTS: We enrolled 28 patients. Everolimus therapy was associated with a clinically meaningful reduction in volume of the primary subependymal giant-cell astrocytoma, as assessed on independent central review ($P < 0.001$ for baseline vs. 6 months), with a reduction of at least 30% in 21 patients (75%) and at least 50% in 9 patients (32%). Marked reductions were seen within 3 months and were sustained. There were no new lesions, worsening hydrocephalus, evidence of increased intracranial pressure, or necessity for surgical resection or other therapy for subependymal giant-cell astrocytoma. Of the 16 patients for whom 24-hour video electroencephalography data were available, seizure frequency for the 6-month study period (vs. the previous 6-month period) decreased in 9, did not change in 6, and increased in 1 (median change, -1 seizure; $P = 0.02$). The mean (\pm SD) score on the validated Quality-of-Life in Childhood Epilepsy questionnaire (on which scores can range from 0 to 100, with higher scores indicating a better quality of life) was improved at 3 months (63.4 ± 12.4) and 6 months (62.1 ± 14.2) over the baseline score (57.8 ± 14.0). Single cases of grade 3 treatment-related sinusitis, pneumonia, viral bronchitis, tooth infection, stomatitis, and leukopenia were reported.

CONCLUSIONS: Everolimus therapy was associated with marked reduction in the volume of subependymal giant-cell astrocytomas and seizure frequency and may be a potential alternative to neurosurgical resection in some cases, though long-term studies are needed. (Funded by Novartis; ClinicalTrials.gov number, NCT00411619.)

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