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Effect of Everolimus on Pediatric Cases of Renal Angiomyolipoma in the EXIST-1 Study

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Objective:
Because everolimus is a systemic therapy and tuberous sclerosis complex (TSC) often affects multiple organs beginning early in life, changes in renal angiomyolipoma volume were explored in a subgroup of patients treated for subependymal giant cell astrocytoma (SEGA) in the EXIST-1 study.

Methods:
Patients with TSC and new or worsening SEGA were randomly assigned (2:1) to receive everolimus 4.5 mg/m2 (target trough 5-15 ng/mL) or placebo. After a double-blind core phase, all remaining patients could receive everolimus in an open-label extension. This post hoc analysis focused on a subset of patients <18 years of age with ≥1 target renal angiomyolipoma at baseline. Response rate was defined as the proportion of patients with ≥50% reduction in renal angiomyolipoma volume from baseline, with neither new lesions ≥1 cm in longest diameter, nor increase in kidney volume ≥20% from nadir, nor angiomyolipoma-related bleeding of grade ≥2. Adverse events (AEs) were monitored continuously.

Results:
In total, 33 patients were included in this analysis. Median duration of everolimus exposure was 44.8 months. Renal angiomyolipoma response rate was 75.8% (95% confidence interval, 57.7-88.9%). From weeks 24 to 144, 100% of patients had ≥30% reduction in angiomyolipoma volume from baseline. The most common AEs (≥25%) were convulsion and mouth ulceration (45.5% each), stomatitis (42.4%), and cough (27.3%).

Conclusions:
Everolimus appears safe and effective for long-term reduction of renal angiomyolipoma volume in patients <18 years of age treated for TSC-associated SEGA.

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