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

John J. Bissler, MD; 1 David N. Franz, MD; 2 Elena Belousova, MD, PhD; 3
Noah Berkowitz, MD, PhD; 4 Thomas Brechenmacher, MSc; 5 Sergiusz Jozwiak, MD, PhD; 6
J. Christopher Kingswood, FRCP, MBBS; 7

1St. Jude Children’s Research Hospital and Le Bonheur Children’s Hospital, Memphis, TN, USA; Royal
Sussex County Hospital, Brighton, UK; 2Cincinnati Children’s Hospital Medical Center, Cincinnati,
OH, USA; 3Moscow Research Institute of Pediatrics & Pediatric Surgery, Moscow, Russia; 4Novartis
Pharmaceuticals Corporation, East Hanover, NJ, USA; 5Novartis Pharmaceuticals S.A.S., Rueil-
Malmaison, France; 6Medical University of Warsaw, Warsaw, Poland; 7Royal Sussex County Hospital,
Brighton, UK

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.

Abstract selected for presentation at 47th ANNA National Symposium, Louisville, KY, 2016