Management of Facial Angiofibroma Related to Tuberous Sclerosis Complex and use of Topical mTOR Inhibitor in the United States: Retrospective Analysis of the Natural History Database

Eric Beresford, PharmD, BCMAS;[1], Steven L. Roberds, Ph.D.;[2] Jo Anne Nakagawa; Sreedevi Boggarapu, Ph.D., CMPP[1]
[1]Nobelpharma America, LLC. 3 Bethesda Metro Center, Bethesda, MD; [2]Tuberous Sclerosis Alliance, Silver Spring, MD

Introduction

- Facial angiofibroma (FA) is the most predominant (74.5% to 83%)[1] cutaneous manifestation of tuberous sclerosis complex (TSC), a genetic disorder impacting the mechanistic target of rapamycin (mTOR) signaling pathway.
- Invasive therapeutic modalities (e.g. surgery and laser therapy) used for treatment of FA are associated with pain, bleeding, and recurrence.[1,2]
- Topical rapamycin formulations, which can provide beneficial effects without systemic exposure and associated risks, were effective in the management of FA,[3–8] however, lack of FDA-approved formulation in the United States is a major limitation.
- This retrospective analysis of the data from the TS Alliance's Natural History Database aimed to evaluate current treatment approaches for management of FA.

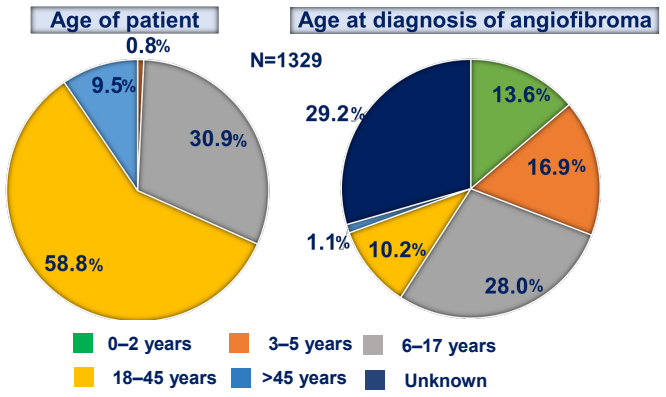
Methods

- The TS Alliance's Natural History Database, the largest repository of longitudinally studied TSC patients, is an IRB-approved research database implemented in 2006.
- In this retrospective analysis, data from patients with FA (n=1329) enrolled in the 18 US-based clinical sites to date were included.

Results

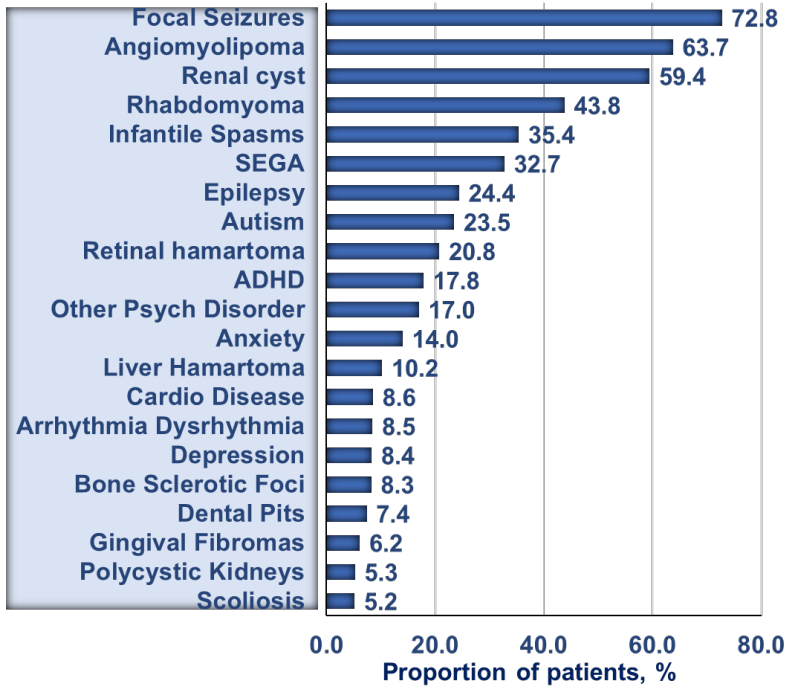
- The median (range) age of participants included in this analysis was 22 (3–86)

Figure 1. Age distributions of patients



- ***Race:*** Majority of patients were white (79.3%), followed by African American (6.4%).
- ***Diagnosis:*** Of the 798 participants who had genetic testing, 517 (64.8%) had TSC2 mutations and 164 (20.6%) had TSC1 mutations

Figure 2. Comorbid conditions related to TSC observed in >5.0% of patients with FA

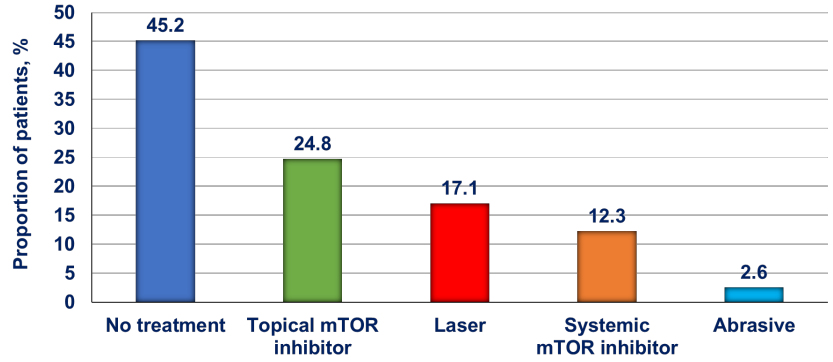


ADHD, Attention-deficit/hyperactivity disorder; SEGA, subependymal giant cell astrocytoma; TSC, tuberous sclerosis complex

Treatment:

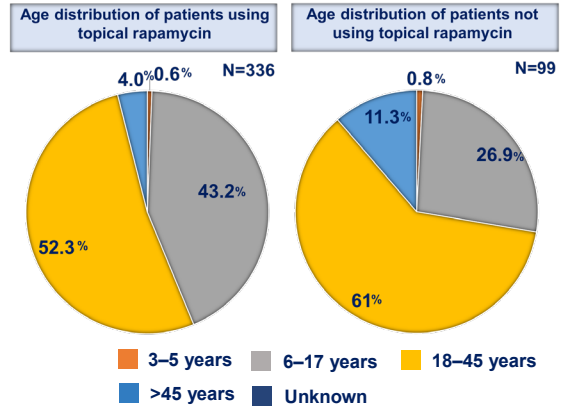
- Although 163 (12.3%) of participants with AF used a systemic mTOR inhibitor, only 16 (1.2%) received systemic mTOR inhibitor exclusively for management of FA.
- Additionally, 222 (16.7%) participants used systemic mTOR inhibitor for other conditions.

Figure 3. Treatments received by patients with facial angiofibroma related to TSC



mTOR, mechanistic target of rapamycin; TSC, tuberous sclerosis complex

Figure 4. Age distributions of patients by topical rapamycin use



- ***Limitations***
  - ***Major limitation:*** This is a retrospective analysis and not prospectively designed to characterize the FA related to TSC.

Conclusions:

- Despite the lack of an FDA-approved formulation, use of topical mTOR inhibitor for the management of facial angiofibroma was observed in nearly 25% of individuals and use of systemic mTOR inhibitor solely for management of facial angiofibroma was observed in a few individuals (1.2%).
- This analysis emphasizes the unmet need for an FDA-approved topical mTOR inhibitor formulation, access to which could benefit many individuals with angiofibroma currently not receiving treatment.

References: 1. Krueger, D. A et al. Pediatric Neurology. 2013;49:255–65; 2. Schwartz RA et al. J Am Acad Dermatol. 2007;57:189–202.; 3. Haemel AK et al. Arch Dermatol. 2010;146:715–8; 4; Wataya-Kaneda M et al. 2020; 5. Wataya-Kaneda M, et al. JAMA Dermatol. 2018;154(7):781-788; 6. Wataya-Kaneda M, et al. JAMA Dermatol. 2017;153(1)39-48; 7. Wheless MC et al. Child Neurol Open. 2019;6:2329048X19835047; 8. Leducq S et al. J Am Acad Dermatol. 2019;80:735-42.

Presented at the 45th annual meeting of SPD, July 10-12, 2020