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# Topical rapamycin combined with pulsed dye laser (PDL) in the treatment of capillary vascular malformations—Anatomical differences in response to PDL are relevant to interpretation of study results

To the Editor: We applaud Marqués et al<sup>1</sup> for their investigation of the use of topical rapamycin combined with pulsed dye laser (PDL) in the treatment of capillary vascular malformations (CVMs) in Sturge-Weber syndrome. Although it is well established that PDL alone can achieve significant improvement in the majority of patients, especially with early treatment, a subset of patients have very modest improvement.<sup>2</sup> There is a clear need for novel treatment modalities and therapeutic techniques to improve clearance rates and treat recalcitrant CVMs.

Early investigation of the use of rapamycin, an inhibitor of mammalian target of rapamycin (mTOR) with antiangiogenic properties, combined with PDL for the treatment of CVMs demonstrated impressive results and generated much excitement and further investigation.<sup>3</sup> While we are hopeful that rapamycin may be used to improve the treatment of CVMs, the investigation by Marqués et all has a critical limitation that may invalidate its conclusions.

In this study the treatment site division and randomization did not control for the well known anatomic differences of CVMs in response to PDL treatment.<sup>4</sup> Centrofacial lesions respond significantly less favorably than CVMs located elsewhere on the head and neck. This is especially true when compared with the temple region, which, in experienced hands, typically responds rapidly to PDL alone. To control for this phenomenon, proper study design necessitates each intervention site be randomized amongst the subjects.

Although the authors of the current study mention this limitation: "PDL was only applied to the lateral parts of the PWS area (not randomly applied to either medial or lateral parts)," it is important that clinicians understand this limitation which may invalidate the conclusions. Although the combined PDL and topical rapamycin approach is intriguing, clinical validation in large numbers of patients with CVM is required. Prospective, comparative, and controlled clinical studies conducted by experienced investigators on a multicenter basis against accepted treatment regimens are required so that the role of topically applied rapamycin in conjunction with PDL therapy of CVM may be fully defined.

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