

ENDORSEMENT

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2024 Canadian Urological Association endorsement of an expert report: Kidney involvement in tuberous sclerosis complex

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The European Rare Kidney Disease Reference Network (ERKNet) has developed comprehensive statements to help patients and clinicians with tuberous sclerosis complex (TSC),¹ as it relates to kidney health.² These broad-ranging statements can aid urologists and other healthcare providers involved in TSC patient care.

The ERKNet Working Group responsible for developing this report consisted of experts from various medical specialties, alongside representatives from patient and family advocacy groups. Their methods are clearly outlined, and the statements cover genetic testing, regular monitoring protocols, and strategies for addressing associated conditions and complications. Statements are assessed using the American Academy of Pediatrics methods, differing from the GRADE approach to guideline development adopted by the Canadian Urological Association (CUA).^{3,4}

In endorsing this expert report, the CUA underscores the following considerations:

1. Many of the statements are primarily based on expert opinions due to the predominance of low-quality evidence underlying them. Nevertheless, this document provides valuable guidance for enhancing the overall medical care of TSC patients.
2. Genetic testing for TSC patients and family members should be guided by a medical geneticist possessing the requisite expertise. High-sensitivity genetic analysis may not be universally accessible across all Canadian centers engaged in genetic testing for TSC patients.
3. The risk factors for increased bleeding risk in patients with TSC have not been validated. Consequently, these proposed factors (Box 4) should serve as triggers to initiate discussions, and treatment decisions should be reached through shared decision-making.
4. We advocate for the management of small renal masses and renal cell carcinoma (RCC) in alignment with existing CUA guidelines.^{5,6} Therefore, contrary to what is stated in the document, we support the role of a biopsy for fat-poor kidney lesions — irrespective of size and growth rate — whenever the biopsy result could potentially impact treatment decisions. We also emphasize the importance of shared decision-making for patients with presumed RCC and recognize the potential role of alternative management approaches, such as active surveillance and thermal ablation.
5. In an effort to optimize adherence and minimize toxicity, the authors of this expert report suggest initiating everolimus in TSC patients at lower doses (5 mg for adults; 2.5 mg/m² for children) in contrast to the doses used in the EXIST-2 (10 mg for adults) and EXIST-1 (4.5 mg/m² in both adults and children) clinical trials;^{7,8} however, it is important to highlight that

while retrospective data suggests equivalence, this has not been rigorously tested.⁹

- Given the diverse healthcare landscape across Canada, the specific physicians involved in caring for TSC patients may vary depending on regional availability and referral patterns. Urologists play a critical role in ensuring comprehensive management of patients with TSC by promoting and facilitating multidisciplinary care. This is particularly relevant for TSC patients undergoing systemic treatment, where managing side effects is paramount. One significant side effect of everolimus not addressed in the document is its potential impact on fertility and breastfeeding. Consequently, patients of childbearing age should receive adequate counselling before starting or while using everolimus.

COMPETING INTERESTS: Dr. Mason has participated in advisory boards for AbbVie, Astellas, Knight, March, Sanofi, Tersera, Tolmar, and Verity; has received speaker honoraria from AbbVie, Bayer, Janssen, and Verity; has received funding for conference travel from Tersera and Verity; and has participated in several clinical trials in prostate, bladder, and testis cancer. Dr. Richard has participated in advisory boards for Astellas, Bayer, and Novartis; has received speaker honoraria from AbbVie, Astellas, Bayer, Janssen, Knight, Novartis, and Tolmar; has participated in a clinical trial supported by Merck; and is on the board of the Kidney Cancer Research Network of Canada. Dr. Bhindi has participated in advisory boards for Bayer, EMD Serono, Ferring, Janssen, and Verity; has received speaker honoraria from Bayer, Merck, and Pfizer; and has participated in a clinical trial supported by Bayer, Elypta AB, and Janssen. Dr. McAlpine has participated in advisory boards for Bayer, Knight, and Tolmar; and has received honoraria from Bayer, Knight, Tersera, and Verity. Dr. Soleimani has participated in advisory boards for Ipsen; has received speaker honoraria from Bayer, Ipsen, and Pfizer; and is a medical advisor for the Canadian VHL Alliance.

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