TSC2 gene

Associated Syndrome Name: Tuberous sclerosis complex (TSC)

TSC2 Summary Cancer Risk Table

CANCER	GENETIC CANCER RISK
Other	High Risk
Other	Elevated Risk
Renal	Elevated Risk

TSC2 gene Overview

Tuberous sclerosis complex (TSC) [1, 2, 3, 4, 5, 6]

- Individuals with *TSC2* mutations have tuberous sclerosis complex (TSC).
- Patients with TSC have an elevated risk for renal cancer, which may be diagnosed at young ages. A high percentage of children with TSC will have some sort of kidney disease due to benign tumors or cysts.
- Though rare, endocrine tumors, such as pancreatic neuroendocrine tumors (PNETs), have been observed in individuals with TSC.
- Patients with TSC often have a wide variety of other, non-malignant features associated with this condition, many of which require medical attention. Benign tumors can occur throughout the body (i.e., angiomyolipoma), including in the skin, brain, kidneys, lungs, and heart. Individuals with TSC frequently have epilepsy and can also be affected by neuropsychiatric conditions such as developmental delay and autism spectrum disorders.
- It is appropriate to offer genetic counseling to individuals with TSC who are of reproductive age to discuss reproductive risks and options. There are additional considerations before and during pregnancy for women with TSC.
- Although there are increased risks for cancer and a high risk for other medical problems in patients with TSC, these risks can be managed with appropriate medical care. Guidelines from the National Comprehensive Cancer Network (NCCN) and the International Tuberous Sclerosis Complex Consensus Group are listed below. Since TSC is a complex condition, patients with *TSC2* mutations and a diagnosis of TSC should be managed by a multidisciplinary team with expertise in medical genetics and the prevention and treatment of the complications associated with this condition.

TSC2 gene Cancer Risk Table

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION
Renal	To age 80[3, 4, 6, 7]	2%-5%	1.5%
Malignant Angiomyolipoma	To age 80[2, 3, 7]	Rare, but elevated risk	<0.1%
Other - Non-malignant features of TSC	All ages[1, 2, 3, 5]	TSC is associated with many life-threatening non-malignant clinical features, some of which may require medical intervention as early as infancy (see Overview).	NA

TSC2 Cancer Risk Management Table

The overview of medical management options provided is a summary of professional society guidelines. The most recent version of each guideline should be consulted for more detailed and up-to-date information before developing a treatment plan for a particular patient.

This overview is provided for informational purposes only and does not constitute a recommendation. While the medical society guidelines summarized herein provide important and useful information, medical management decisions for any particular patient should be made in consultation between that patient and his or her healthcare provider and may differ from society guidelines based on a complete understanding of the patient's personal medical history, surgeries and other treatments.

CANCER TYPE	PROCEDURE	AGE TO BEGIN	FREQUENCY (UNLESS OTHERWISE INDICATED BY FINDINGS)
Renal	Abdominal MRI (preferred) or CT, with and without contrast[5]	12 years, or individualized to a younger age based on the earliest renal cancer diagnosis in the family	Every 1 to 3 years
Malignant Angiomyolipoma	Blood pressure monitoring[1, 8]	Individualized	Annually
	Biochemical screening of blood and urine[1, 8]	Individualized	Annually
	Abdominal ultrasound[8]	At time of diagnosis of TSC	Every 1 to 3 years until age 12
	Abdominal MRI[1, 3]	Baseline at time of diagnosis of TSC, then ongoing screening starting at age 12	Every 1 to 3 years
	Consider everolimus therapy for asymptomatic, growing angiomyolipoma measuring >3 cm in diameter.[3, 5]	Individualized	NA
Other - Non-malignant features of TSC	Multiple screenings recommended, which may include comprehensive physical exam, brain MRI, echocardiogram, chest CT, eye and skin exam, and evaluations for neuropsychiatric disorders.[1, 3]	At time of diagnosis of TSC	Varies

Information for Family Members

The following information for Family Members will appear as part of the MMT for a patient found to have a mutation in the TSC2 gene.

This patient's relatives are at risk for carrying the same mutation(s) and associated cancer risks as this patient. Cancer risks for females and males who have this/these mutation(s) are provided below.

Family members should talk to a healthcare provider about genetic testing. Close relatives such as parents, children, brothers and sisters have the highest chance of having the same mutation(s) as this patient. Other more distant relatives such as cousins, aunts, uncles, and grandparents also have a chance of carrying the same mutation(s). Testing of at-risk relatives can identify those family members with the same mutation(s) who may benefit from surveillance and early intervention.

Approximately two-thirds of individuals with TSC have not inherited the *TSC2* mutation from a parent. In these cases the mutation has developed spontaneously in that individual (a *de novo* mutation). Once this occurs, the children of that individual are each at 50% risk of inheriting the mutation.[1, 2, 3]

Since *TSC2* mutations carry a risk for complications in children and some screenings are recommended to begin in infancy, mutation testing should occur as soon as a diagnosis of TSC is suspected.[1, 2, 3]

It is appropriate to offer genetic counseling to individuals with TSC who are of reproductive age to discuss reproductive risks and options. There are additional considerations before and during pregnancy for women with TSC.

References

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