UT Southwestern
Harold C. Simmons
Comprehensive Cancer Center

NCI Designated Comprehensive Cancer Center

*SMARCA4 M*utations

What You Should Know About *SMARCA4* Mutations

SMARCA4 gene mutations are associated with varying cancer risks and other features depending on the specific mutation. Certain mutations in *SMARCA4* have an increased risk for rhabdoid tumor predisposition syndrome (RTPS). Rhabdoid tumors are tumors of the soft tissue that most often occur in the kidney, brain, and nervous system but may be found in other soft tissues as well. Rhabdoid tumors are most common in infancy or childhood. Females with RTPS also have an increased risk for small cell carcinoma of the ovary. Other mutations in *SMARCA4* cause a condition called Coffin-Siris syndrome, which is associated with developmental delay, distinct facial features, low muscle tone, and malformation of certain organs at birth.

Cancer Risks Associated with a *SMARCA4* Mutation

- Rhabdoid Tumors: Malignant tumors (cancerous growths of cells) which occur most commonly in infancy. These tumors most commonly start in the kidneys, but have also been seen in the brain. When these tumors are seen in the brain they are known as atypical teratoid/rhabdoid tumors (AT/RTs). These tumors are aggressive and require immediate medical care.
- Ovarian Cancer: Females with *SMARCA4* mutations have an increased risk for a rare type of ovarian cancer in known as small cell carcinoma of the ovary, hypercalcemic type (SCCOHT; also known as a malignant rhabdoid tumors of the ovary). This is an aggressive type of ovarian cancer that can be seen at any age, even in infancy; however, it appears most commonly in young women with the median age of 27 years. SCCOHT tumors are characterized by increased blood calcium levels.

Risks to Family Members

Mutations in the *SMARCA4* gene are inherited in an autosomal dominant fashion. This means that children, brothers, sisters, and parents of individuals with a *SMARCA4* mutation have a 1 in 2 (50%) chance of having the mutation as well. Individuals with a *SMARCA4* mutation may develop a rhabdoid tumor, ovarian cancer, other cancers/tumors, or none of the above. Both males and females can inherit a familial *SMARCA4* mutation and can pass that it on to their children.

Managing Cancer Risks

There are no formal recommendations for surveillance of individuals with a *SMARCA4* mutation. In individuals who have *SMARCA4* mutations and cancer, immediate medical attention and aggressive therapy are important. Therapies are based on institutional/treating physician preferences combining surgery, radiotherapy, and chemotherapy. As mutations in *SMARCA4* are rare, screening for individuals with *SMARCA4* mutations may be tailored to each individual's personal and family history. The AACR Pediatric Oncology Series has published the following recommendations for individuals with a *SMARCA4* mutation:

- Rhabdoid Tumors: no screening recommendations at this time.
- Ovarian Cancer: abdominal ultrasounds every 6 months may be considered for younger women and prophylactic oophorectomies are recommended for older women with consideration of the family history, reproductive plans, emerging data, and age.

Last updated 01/09/2020

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