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Provincial Health Services Authority

Li-Fraumeni Syndrome - *TP53* Cancer Risks and Management

Overview

Li Fraumeni Syndrome (LFS) is an inherited condition that increases the risk of certain cancers. It is caused by pathogenic variants in the *TP53* gene. This document summarizes the cancer risks and management recommendations for individuals with a confirmed *TP53* pathogenic variant.

Cancer risks associated with *TP53*

The tumours seen most in families with LFS include **premenopausal breast cancer** and **sarcomas** (soft tissue and bone). Other characteristic cancers include **brain tumours**, and **adrenocortical carcinoma (ACC)**. A wide range of additional cancers can also be seen, including leukemia, lymphoma, lung, prostate, colon, gastric, pancreatic and melanoma.

LFS tumours typically occur at younger ages than in the general population, with diagnoses ranging from early childhood to adulthood. Age related patterns include:

- 0 –10 years: soft-tissue sarcomas, brain tumours, ACC
- 11–20 years: bone sarcomas
- >20 years: female breast cancer, brain tumours

Estimating cancer risks for an individual with LFS is challenging because published risk estimates vary widely, and clinical expression differs between and within families. It is important to recognize that much of LFS literature is biased towards families meeting classic diagnostic criteria or those with high cancer incidence. Individuals with LFS have an increased risk of developing multiple primary tumours. The risk for a second cancer is approximately 50% within 10 years after the first diagnosis.

Risk of cancer by age	**15 years**	**30 years**	**45 years**	**60 years**
Males	15-25%	20-40%	40-60%	>70%
Females	5-15%	40-50%	75-90%	>90%

Cancer Screening and Risk Reduction

Adults (18 years and older)	
Area	**Recommendation**
General	Complete physical exam every 6 months Prompt evaluation with primary care provider for any medical concerns
Breast Cancer	Breast awareness from first development Clinical breast exam every 6–12 months starting at 20–25 years Annual breast MRI* age 20–75 (ultrasound if pregnant/lactating) Consider risk-reducing bilateral mastectomy (<40 yrs gives most benefit).
Brain Tumour	Annual brain MRI (first with contrast; subsequent without if normal).
Soft Tissue & Bone Sarcoma	Annual whole-body MRI (WBMRI)* Annual abdominal/pelvic ultrasound*
Lung	Radiologists to be vigilant for lung lesions as part of WBMRI. Low-dose chest CT scans have not been assessed in LFS. Low and ultralow-dose CT may be used following lung lesion detection.
Prostate	Annual prostate-specific antigen (PSA) testing and digital rectal examination starting at age 35
Gastrointestinal Cancers	Upper endoscopy and colonoscopy every 2–5 yrs from age 25 yrs (or 5 yrs before earliest diagnosis in family)
Pancreatic Cancer	Diabetes screen (fasting glucose or HbA1C) every 3 years from age 40. Investigate new onset of diabetes or unexplained changes in diabetic control; consider pancreatic imaging and refer to GI specialist if any abnormalities. Additional pancreatic screening may be recommended to people who have a close relative with pancreatic cancer and *a TP53* pathogenic variant. There is more information here: HCP_GuidelinesManuals_FamilialPancreaticCancer.pdf
Melanoma	Annual skin examinations by a dermatologist

* Breast MRI and abdominal/pelvic ultrasound to alternate with WBMRI to ensure **one scan every 6 months.**

Children (birth to age 18 years)	
Area	**Recommendation**
General Assessment	Physical exam every 3–4 months, including: blood pressure; weight, height, waist/hip circumference plotted on growth curves (monitor for rapid acceleration); assessment for Cushingoid features; virilization signs (pubic hair, axillary moisture, adult body odor, androgenic hair loss, clitoromegaly, penile growth); full neurologic exam Skin exam with low threshold for formal dermatologic exam for any uncertain or suspicious nevi Prompt primary-care assessment for any new concerns
Adrenocortical Carcinoma (ACC)	Abdominal/pelvic ultrasound every 3–4 months
Brain Tumour	Annual brain MRI (first with contrast; subsequent without if normal)
Soft Tissue & Bone Sarcoma	Annual whole-body MRI (WBMRI)

General Recommendations for Children and Adults with LFS

- Have a designated clinician responsible for coordinating cancer prevention, surveillance, and expedited assessment when new symptoms arise.
- Ensure prompt investigation of persistent or unexplained symptoms (e.g., headaches, limb or bone pain, abdominal discomfort).
- Maintain healthy lifestyle practices: avoid smoking, exercise regularly, maintain a weight that supports overall health, limit alcohol intake, and minimize excessive sun exposure.
- Avoid unnecessary radiation exposure (e.g., minimize non-essential x-rays), but do not delay or avoid medically necessary diagnostic or therapeutic radiation.

Note: In the information above, male/female refers to sex assigned at birth.

High Risk Clinic

Individuals who carry a pathogenic variant in the *TP53* gene, or are at 50% risk of having inherited one, can be referred to the Hereditary Cancer Program's High Risk Screening Clinic for ongoing cancer risk management and decision support. Read more about the High Risk Clinic.

Family and Reproductive Considerations

Inheritance

Each child of someone with a *TP53* pathogenic variant has a 50% chance of inheriting the variant.

Family members are encouraged to contact their local genetics clinic to learn more about whether genetic testing or cancer screening may be helpful for them. Family members who live in British Columbia or the Yukon can contact our program directly at hereditarycancer@bccancer.bc.ca.