# Li-Fraumeni Syndrome Education and Early Detection Clinic

**Making a difference in quality of life and long-term survival through screening and education**

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## Introduction

Li-Fraumeni Syndrome (LFS) is a genetic cancer predisposition syndrome that is defined as any germline mutation in the TP53 tumor suppressor gene. It is passed down in an autosomal dominant pattern, with a 50% chance of passing the mutated gene to each child. In response to stress signals, the tumor suppressor gene controls a wide range of processes including apoptosis, DNA replication and repair, and regulatory control over the cell cycle. When this gene is mutated, cells lack control over these processes. There are two different types of criteria used to diagnose LFS, the classical and the Chompret criteria, which are defined by patients with first degree relatives diagnosed with particular cancers at certain ages. There are certain cancers that are associated with LFS, and prevalence of these cancers varies based on age. In the pediatric/young adult population, risk is highest for sarcomas, brain tumors, adrenocortical carcinoma, leukemia, and early onset breast cancer. Cumulative cancer risk associated with LFS has been estimated to be approximately 50% by age 40 years and up to 90% by age 60 years.

Patients are recommended to follow regular surveillance screening guidelines, which have been shown to improve overall survival. Multiple screening guideline protocols are utilized, including that of the MD Anderson Children's Cancer Hospital pediatric LEAD clinic. LFS can have a significant physical and psychological impact on children and families that it effects.

## Practice

The mission of the LEAD program at MDACC is to improve the patient experience, quality of life, and long-term survival for children diagnosed with LFS by providing age-appropriate screening and supportive care services from professionals with LFS expertise in a dedicated program.

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### Li-Fraumeni Syndrome Screening - Pediatric

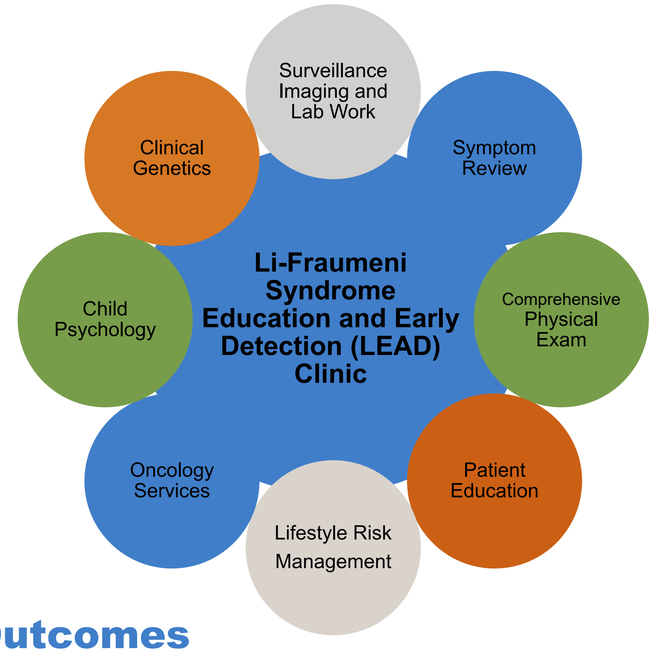
Disclaimer: *This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care.*

**Li-Fraumeni Syndrome Education and Early Detection (LEAD) – Pediatric Screening Guidelines**

| Cancer | Age | | | Frequency |
|---|---|---|---|---|
| | 0-1 Year | 1-10 Years | 10-20 Years | |
| General | Physical exam/targeted review of systems<br>• Neurological exam | Physical exam/targeted review of systems<br>• Neurological exam | Physical exam/targeted review of systems<br>• Neurological exam • Thyroid • Skin | Every 6 months |
| Adrenocortical Tumor (ACT) and Others | • Education of signs and symptoms (virilization, Cushing's syndrome, hypertension)<br>• Testosterone, DHEAS, HCG, AFP, ACTH, urinalysis | • Education of signs and symptoms (virilization, Cushing's syndrome, hypertension)<br>• Testosterone, DHEAS, HCG, AFP, ACTH, urinalysis | • Education of signs and symptoms (virilization, Cushing's syndrome, hypertension)<br>• Testosterone, DHEAS, HCG, AFP, ACTH, urinalysis | • Every 6 months (until 10 years old)<br>• Annually (10 – 20 years old) |
| | Ultrasound of abdomen and pelvis | Ultrasound of abdomen and pelvis | Whole body MRI[1] | • Every 6 months for ultrasound<br>• Annually for whole body MRI[1] |
| Brain | • Education of signs and symptoms (vomiting, headaches, vision changes)<br>• Brain MRI[1,2] | • Education of signs and symptoms (vomiting, headaches, vision changes)<br>• Brain MRI[1,2] | • Education of signs and symptoms (vomiting, headaches, vision changes)<br>• Brain MRI[1,2] | Annually |
| Sarcoma (begin at 2-3 years – based on family history/clinical judgement) | N/A | Whole body MRI[1] | Whole body MRI[1] | Annually |
| Leukemia/ Lymphoma | • Education of signs and symptoms (anemia, pallor, fatigue, bruising, petechiae)<br>• CBC, erythrocyte sedimentation rate, lactate dehydrogenase | • Education of signs and symptoms (anemia, pallor, fatigue, bruising, petechiae)<br>• CBC, erythrocyte sedimentation rate, lactate dehydrogenase | • Education of signs and symptoms (anemia, pallor, fatigue, bruising, petechiae)<br>• CBC, erythrocyte sedimentation rate, lactate dehydrogenase | • Every six months (until 10 years)<br>• Annually (10 – 20 years old) |
| Melanoma | N/A | N/A | Refer to Dermatology service as necessary | Annually |

[1]BUN and creatinine prior to any MRI
[2]First MRI with contrast; thereafter without contrast if previous MRI normal and no new abnormality

- This program provides a comprehensive evaluation and needs assessment for the LFS pediatric population at MDACC. It is individualized to the patient with a multidisciplinary team offering health screening and supportive education. Individualized recommendations and referrals are placed based on the assessment outcomes.
- Program services begin with a personal or family history of LFS. The patients are then referred for genetic testing. If the testing indicates a germline TP53 mutation, then the patient is referred to the LEAD clinic to begin screening.
- In the LEAD clinic, patients begin with an assessment and evaluation, including a complete history and physical exam. They then undergo the appropriate screening (including MRI whole body, MRI brain, ultrasounds, lab work, and dermatology assessments). Patients are provided education on signs/symptoms to watch for, lifestyle risk management and psychologic evaluation.
- If a malignancy is identified, patients are referred to the appropriate oncology team for treatment. Screening for LFS continues during treatment, when possible.
- It can be challenging to get appropriate imaging approved with insurance companies, in particular the MRI whole body, as they perceive screening to be investigational.




## Outcomes

At this time, 224 pediatric patients have been tested for TP53 mutations at MDACC, and 34 have tested positive for LFS. There are currently ~20 patients receiving care in the MDACC pediatrics LEAD clinic. Of those 18, five patients have received treatment for at least one malignancy. Once a patient turns 21, they transition to our adult LEAD clinic, as they focus on additional malignancies that affect the adult population.

## References

Amadou, A., Achatz, M.I. W., Hainaut, P. (2018). Revisiting tumor patterns and penetrance in germline TP53 mutation carriers: temporal phases of Li-Fraumeni syndrome. *Curr Opin Oncol*, *30*(1), 23-29.

Bojadzieva, J., et al. (2018). Whole body magnetic resonance imaging (WB-MRI) and brain MRI baseline surveillance in TP53 germline mutation carriers: experience from the Li-Fraumeni Syndrome Education and Early Detection (LEAD) clinic. *Familial Cancer*, *17*(2), 287-294.

Mai P. L., et al. (2016). Risks of first and subsequent cancers among TP53 mutation carriers in the National Cancer Institute Li-Fraumeni syndrome cohort. *Cancer, 122*(23), 3673-3681.

National Comprehensive Cancer Network. Li-Fraumeni Syndrome. https://www.nccn.org/professionals/physician_gls/pdf/lifraumeni.pdf. Accessed January 27, 2020.

Villani A., et al. (2016). Biochemical and imaging surveillance in germline TP53 mutation carriers with Li-Fraumeni syndrome: 11 year follow-up of a prospective observational study. *Lancet Oncol, 17* (9):1295-305.

Special Acknowledgement:
Jessica Corredor, MS, CGC Genetic Counselor