Li-Fraumeni Syndrome (LFS) Fact Sheet for Medical Providers

- LFS is a hereditary cancer predisposition syndrome caused by inherited or de novo pathogenic variants (also called mutations) in one copy of the TP53 tumor suppressor gene, present in the patient from birth (i.e. germline variant).
- People with LFS only have one fully functional TP53 gene to protect against accumulation of further cancer-causing genetic mutations.
- Risk for rare and common cancers is significantly elevated for both children and adults with LFS, leading to significant screening recommendations. Below: Approximate percentage of males and females with a first primary cancer by age (PMIDs: 21779515, 27496084) and summary of recommended screening modalities by age.

<table>
<thead>
<tr>
<th>Age</th>
<th>Abdominal Ultrasound</th>
<th>Complete Physical +/- Bloodwork</th>
<th>Whole-body MRI</th>
<th>Brain MRI</th>
<th>Dermatology</th>
<th>Endoscopy/Colonoscopy</th>
<th>Breast MRI (Females)</th>
<th>Mammogram (Females)</th>
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</thead>
<tbody>
<tr>
<td>15 years</td>
<td>Pediatric</td>
<td>All ages; peds: q3-4 mos; adults: annual</td>
<td>All ages annual</td>
<td>All ages annual</td>
<td>18+ years annual</td>
<td>25+ years q2-5 yrs</td>
<td>20-75 years annual</td>
<td>30-75 years annual</td>
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<td>30 years</td>
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<td>45 years</td>
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<td>60 years</td>
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- The most common cancers seen in LFS are premenopausal breast cancer, soft tissue sarcoma and osteosarcoma, brain cancer, and adrenocortical carcinoma (especially pediatric). Hematological cancers are also common.
- Not everyone with LFS will develop a cancer; others will develop multiple cancers.
- Medical Providers caring for patients with LFS should:
  - Maintain a high index of suspicion of malignancy during office visits.
  - Be familiar with LFS cancer screening recommendations and coordinate with other specialists as necessary to ensure the patient has access to appropriate screening.
  - Connect the patient with an LFS clinic or a local provider who is willing to coordinate recommended screening scans, including annual whole-body MRI or a suitable alternative if whole-body MRI is unavailable.
  - Avoid ordering scans involving radiation except when medically necessary.
  - Be cognizant of psychological stresses individuals with LFS may experience both chronically and acutely, particularly surrounding periods of screening or diagnosis, and consider referral to a mental health provider as necessary.

MORE INFORMATION

SUMMARIES
UpToDate: https://www.uptodate.com/contents/li-fraumeni-syndrome
PubMed PMIDs: 21779515, 27496084, 26014290, 29076966

QUESTIONS & SUPPORT
Your institution’s cancer genetic counselor
A local cancer genetic counselor (https://www.findageneticcounselor.org)
Li-Fraumeni Syndrome Association (LFSA) Genetic Counseling Advisory Group and Medical Advisory Board
https://www.lfsassociation.org/genetic-counseling-advisory-group/
https://www.lfsassociation.org/medical-advisory-board/

SCREENING GUIDELINES
Adult: NCCN Guidelines: Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic
Whole Body MRI Publications: PMIDs: 33151095, 28572262, 28772291

LFS CLINICS
https://www.lfsassociation.org/medical-resources/; https://www.lfsassociation.org/medical-resources/treatment-facilities/

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