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Lessons learnt from clinico-genomic profiling of families with Li Fraumeni Syndrome: the largest case series from the Indian setting

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Background

- **Inherited cancer predisposition syndrome** due to TP53 germline mutations[1]
- Encompasses a **wide spectrum of cancers** such as breast cancers, sarcomas, leukemias, adrenocortical carcinomas, brain tumors
- Accords cumulative cancer risk[2] of 46% by 50 years and **almost 100% by 70 years**
- Diagnostic criteria include Classical criteria[3], Chompret criteria and others e.g. Birch's, Eel's criteria
- **Sparse Indian data** – limited resources/less awareness/reluctance among patients for testing

Study Objectives and Methods

- Study the clinico-epidemiologic and genetic profile of patients and their family diagnosed with LFS
- Characterize the TP53 mutations diagnosed in the families with LFS
- **Retrospective study** conducted by review of hospital records
- Included patients with LFS along with their families, who were registered at our sarcoma medical oncology clinic between September 2015 and 2022

Declarations & Correspondence information

- No conflict of interest to declare; no funding received
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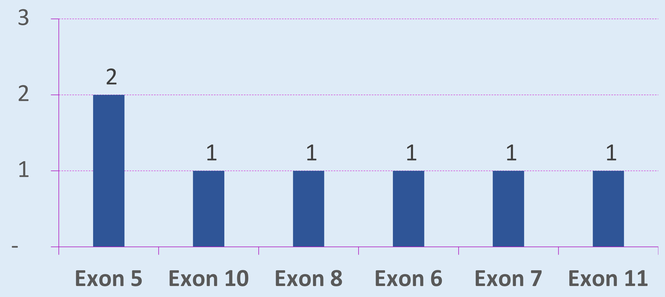
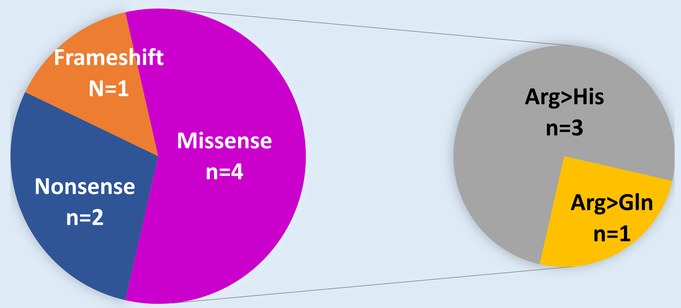
Results

Patient characteristics	
Median age of index cases (range)	22 years (9-63)
Median age of tumor onset in overall cohort (range)	40 years (9-70)
Gender distribution (n, %)	Male (11, 47.8%) Female (12, 52.1%)
Spectrum of malignancies	1. Sarcoma (9, 39.71% pts) 2. Breast (4, 17.3% pts) 3. Leukemia (2, 8.7% pts) 4. Head and neck cancer(2, 8.7%)

- 7 families with 23 cancer patients and 5 asymptomatic carriers
- **TP53 mutation positive in 8 cancer patients, rest deceased**
- Median of 3 cancers (range 2-5) per family
- **2 index cases had dual primary malignancies**
- 1 pediatric case of metastatic Adrenocortical carcinoma

TP53 mutational profile





Unique challenges encountered

- 2 families met diagnostic criteria prior to onset of cancer in index case – **a window missed**
- 4 families started Toronto protocol-based surveillance **– 1 dropped out due to financial pressure/social stigma**
- Grief, anxiety, resistance to testing and surveillance among patients
- When to perform biopsies in "probably" benign screen-detected lesions?
- Pre-implantation genetic testing among mutation carriers?