FAQ-Protocol 4
TP53 testing and management guidelines
Frequently asked questions

Last updated: 09/02/2015

Q: What is Li-Fraumeni syndrome?
Li-Fraumeni syndrome (LFS) describes a clinically defined cancer predisposition syndrome originally reported in 1969. The classic clinical criteria are given in Protocol 4, box 3. Families with Li-Fraumeni syndrome have a predominance of sarcomas, breast, brain and adrenocortical tumours which occur at young ages, although many other cancers can also occur. Approximately 70% of families who meet classic LFS criteria have a germline mutation in TP53. TP53 mutations have also been identified in families who do not fulfil classic criteria and these are sometimes called “LFS-like”. It is unclear if these families have the high cancer risks associated with classic LFS (see also below).

Q: If a TP53 mutation is identified in a family, does this mean they have LFS?
No. As more individuals and families have been tested for TP53 mutations, it has become clear that the spectrum of clinical features is broad and many families do not meet the classic LFS criteria and may not be at the same high risk of cancer. The term Li-Fraumeni syndrome should be restricted to those families that meet the classic LFS criteria.

Q: What cancers are typically associated with a TP53 mutation?
Four “core” cancers are typically associated with a TP53 mutation. These are sarcoma (osteosarcoma, soft-tissue sarcoma, rhabdomyosarcoma etc.), breast cancer, brain cancer (e.g. glioma, meningioma etc) and adrenocortical cancers. Many other cancers have been reported in TP53 mutation carriers including leukaemia, pancreatic, ovarian, colon, Wilms tumor and others. The full spectrum and risks of cancers associated with TP53 mutations are currently unknown as testing has been highly selective.

Q: What cancer risks are associated with a TP53 mutation?
It is important to counsel all carriers within the context of the family history. Penetrance of TP53 mutations for proven carriers has only been determined by one small study, consisting of 13 TP53 carriers who were ascertained from a childhood cancer series and therefore likely to represent a more severe phenotype (cancer risks were estimated at up to 70% in males and 100% in females). No population based studies of penetrance have been performed.

Cancer risks for TP53 carriers are likely to be influenced both by the family history and the position and type of mutation. Please email vus@icr.ac.uk for information regarding specific mutations.

Q: Why is there no surveillance for cancers other than breast cancer?
Breast cancer is the only TP53-related malignancy for which effective surveillance exists. No screening modalities have been identified to be of benefit in early detection of sarcoma, brain or adrenocortical cancer. Abdominal ultrasound to screen for adrenocortical cancer has not been shown to be effective and should not be offered. Although leukaemia was described in the original LFS families, it has since been demonstrated to have only a weak association with TP53 mutations. Annual blood films are not recommended, the false positive rate is high and there is no evidence that it is an effective screening modality.