Protocol 4
TP53 mutation testing and management guideline

- Individuals affected with cancer and meeting one of the categories below are eligible for TP53 testing.
- **Relative** = first degree relative or second degree relative.
- **Sarcoma** = bone or soft-tissue sarcoma.

**One individual affected with**

- Adrenocortical cancer at any age
- Choroid plexus cancer at any age
- Rhabdomyosarcoma below 5 yrs
- Breast cancer below 30 yrs
  (if eligible for BRCA testing, this should be performed first)
- Two or more primary cancers of the following: sarcoma, breast, brain, adrenocortical or any childhood cancer; at least one below 46 yrs
  (with the exception of two breast cancers)

**Two relatives affected with**

- Sarcoma, breast, brain, adrenocortical or any childhood cancer;
  one relative below 36 yrs and one relative below 46 yrs
  (with the exception of two breast cancers)

**Three relatives affected with**

- Sarcoma below 45 yrs
  and
- any cancer below 45 yrs
  and
- any cancer below 45 yrs or sarcoma at any age

**Cancer risks for TP53 carriers***

- Families with a history of classic Li-Fraumeni syndrome should be counselled that the lifetime risk of cancer is high (estimated up to 70% in males and up to 90% in females).
- Cancer risks in families without a history of classic Li-Fraumeni syndrome may be lower.
- Cancer risk may be influenced by the type and position of the mutation. Please contact vus@icr.ac.uk for further information about specific mutations.

**Management for TP53 carriers and those at 50% risk***

- Open door policy (can be with a general paediatrician or paediatric oncologist for children).
- Breast cancer risk management should include:
  - Practice of breast self-awareness and self-examination
  - annual MRI age 20-50 yrs, review at age 50
  - discussion of risk-reducing mastectomy
- No targeted surveillance is recommended or of proven benefit other than for breast cancer.
- Cancer treatment should be the optimal treatment for the specific cancer. Radiotherapy should only be avoided if another treatment modality is of equal or superior benefit.
- Predictive testing after appropriate counselling can be undertaken at any age.

* See FAQ document for further details http://www.icr.ac.uk/protocols

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