

New ERN GENTURIS guidelines on heritable TP53-related cancer syndrome and PTEN hamartoma tumour syndrome

ERN GENTURIS

- Patients with genetic tumour risk syndromes (genturis) are at high risk of developing tumours in multiple organ systems at a young age.
- Early identification and diagnosis are the critical factors to improve prognosis and access to appropriate and timely management.
- There are > 40 different genturis, including TP53-related cancer syndrome (hTP53rc, **Li-Fraumeni syndrome**) and PTEN hamartoma tumour syndrome (PHTS, **Cowden syndrome**).

The unmet need for patients as well as professionals includes the lack of national or European guidelines, for these rare diseases, that fit into our European healthcare systems.

Method

- We established two separate multidisciplinary teams of experts representing all relevant disciplines and patients' representatives.
- 337 (hTP53rc) and 131 (PHTS) published articles were assessed in the guideline development.
- The guidelines were based on the best evidence and expert consensus.
- A lay-persons' version and a 'pocket guide' was also developed.

hTP53rc

Recommendations

For age < 18 years, recommendations include:

- Clinical examination and abdominal ultrasound biannually.
- Where individuals harbour a TP53-pathogenic variant, known to be associated with childhood cancers, annual whole-body-MRI and brain-MRI from the first year of life is recommended.

In adults (18+), the surveillance protocol includes:

- Annual clinical examination.
- Annual whole-body-MRI.
- Annual breast-MRI in females from 20 until 65 years.
- Annual brain-MRI until 50 years.

Surveillance Protocol for Heritable TP53-related cancer syndrome (hTP53rc)

Exam	Periodicity	Age to Start	Age to End	Condition	Evidence
Clinical examination with, in children, specific attention to signs of virilisation or early puberty, and measurement of arterial hypertension and, in patients who received radiotherapy, to occurrence of basal cell carcinomas within the radiotherapy field.	Every 6 months	Birth	17 years		Moderate
	Annual	18 years	-		Moderate
Whole-Body MRI	Annual	Birth	-	High cancer risk TP53 variant or previously treated by chemotherapy or radiotherapy.	Moderate
		18 years	-		Strong
Breast MRI	Annual	20 years	Until 60-70 years		Strong
Brain MRI*	Annual	Birth	18 years		Moderate
		18 years	Until 60-70 years	High cancer risk TP53 variant	Moderate
Abdominal ultrasound	Every 6 months	Birth	Until 18 years		Strong
Urine steroids**	Every 6 months	Birth	Until 18 years		Weak
Colonoscopy***	Every 5 years	18 years	-		Weak

*The first scan should be conducted with iv. Gadolinium enhancement; brain MRI should alternate with the WBMRI, so that the brain is imaged at least every 6 months.
**When abdominal ultrasound does not allow a proper imaging of the adrenal glands.
***Only if the carrier received abdominal radiotherapy for the treatment of a previous cancer, or if there is a familial history of colorectal tumours suggestive of an increased genetic risk.

Cancer Surveillance Protocol for individuals with PTEN hamartoma tumour syndrome (PHTS)

Surveillance	Interval	From Age	Evidence	
Breast cancer	MRI	Yearly	30	Strong
	Mammography	Every 2 yrs.	40	Moderate
	Risk reducing surgery offered	-	-	Strong
Thyroid cancer	Ultrasound	Yearly	18*	Strong
Renal cancer	Ultrasound	Every 2 yrs.	40	Moderate
Colorectal cancer	Baseline colonoscopy	-	35-40	Moderate
Melanoma	Baseline skin examination**	-	30	Weak
Endometrial cancer***	Not recommended	-	-	Weak

*Moderate evidence for age of commencement of surveillance. ** Consider further surveillance as required. ***Consider surveillance as part of clinical trial.

PHTS

Recommendations

- Thyroid cancer annual ultrasound from age 18.
- Renal cancer ultrasound two-yearly, from age 40.
- Colorectal cancer baseline colonoscopy at age 35-40
- Melanoma baseline skin examination at age 30.

