**General information**

- Germline pathogenic variants (GPV - including class 4 likely pathogenic and class 5 pathogenic variants) in *BAP1* are associated with BAP1-associated tumour predisposition syndrome (BAP1-TPDS) (OMIM #614327) and follow an autosomal dominant inheritance pattern.
- *BAP1* heterozygotes (carriers) are at increased lifetime risk of pleural and peritoneal mesothelioma, renal cell carcinoma, uveal and cutaneous melanoma and BAP1-inactivated melanocytic tumours (BIMT), which are considered core BAP1-TPDS cancers/tumours.
- The lifetime risk of developing meningioma is likely increased, but meningioma is not currently considered a core associated tumour. Further evidence is required to confirm an association for hepatocellular carcinoma, cholangiocarcinoma or other cancers.
- There is not currently a clear association for any specific histological subtypes of cancer, although an association with rhabdoid type meningioma has been suggested.
- The overall lifetime risk of cancer is estimated to be up to 85%, but this risk may be overestimated due to ascertainment bias.
- The age of onset of cancer is typically younger than in the general population with potentially poorer outcomes for uveal, cutaneous melanoma and renal cell carcinoma. Conversely there is some evidence that *BAP1* heterozygotes with mesothelioma have a better prognosis.

**Associated cancer risks**

<table>
<thead>
<tr>
<th>Tumour Type</th>
<th>Lifetime Risk</th>
<th>Mean Age (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesothelioma</td>
<td>≈ 20%</td>
<td>50s-60s (40-70 years)</td>
</tr>
<tr>
<td>Uveal melanoma</td>
<td>≈ 25%</td>
<td>50s (15-80 years)</td>
</tr>
<tr>
<td>Cutaneous melanoma</td>
<td>≈ 20%</td>
<td>40s-50s (20-80 years)</td>
</tr>
<tr>
<td>Renal cancer</td>
<td>5-10%</td>
<td>Early 40s (35-70 years)</td>
</tr>
</tbody>
</table>

**Management recommendations**

**Surveillance**

- **Renal**: Annual renal imaging from age 30 years. The preferred modality of renal imaging is MRI. If unavailable, renal ultrasound scan can be used as an alternative. MRI is recommended for ongoing surveillance of a known lesion. Refer to local Clinical genetics for recommendations on organisation of renal cancer surveillance.
- **Uveal melanoma**: Annual dilated ophthalmic examination by an ocular oncologist or an ophthalmologist with expertise in uveal melanoma is recommended from age 16-18 years.
- **Cutaneous melanoma**: Annual dermatological review including full body examination and photography is recommended from age 18-20 years.
- **Mesothelioma**: Surveillance is not currently recommended as neither chest X-ray or MRI have been demonstrated to detect mesothelioma at an early stage. Prospective studies of surveillance in *BAP1* heterozygotes are required and therefore at present, surveillance for mesothelioma should only be undertaken in the setting of a research study. Patients should be advised on symptom awareness with low threshold for investigation.

**Lifestyle advice**

- Provide information on avoiding occupations with asbestos exposure and being aware of residential exposure during renovations.
- Provide information on sun protection and self-examination of skin.
- Provide information on the benefits of smoking cessation, minimising alcohol intake and maintaining a healthy weight to lower the chance of getting cancer.

**Family matters**

- Refer to clinical genetics for discussion of predictive genetic testing in at-risk family members.
- Predictive testing is normally considered from around the age at which surveillance starts (approx. age 16-18 years).
- Refer to clinical genetics for discussions on reproductive options.

**References**

- Laloo et al., 2023 [https://doi.org/10.1038/s41431-023-01448-z](https://doi.org/10.1038/s41431-023-01448-z)
- Walpole et al., 2018 [https://doi.org/10.1093/inci/dqy171](https://doi.org/10.1093/inci/dqy171)
- Chau et al., 2019 [https://10.3390/cancers11081114](https://10.3390/cancers11081114)

**Patient resources**

- [https://genomel.org/info-for-patients/the-bap1-interest-group-big-consortium/](https://genomel.org/info-for-patients/the-bap1-interest-group-big-consortium/)