# BMPR1A Germline Pathogenic Variant Carriers: Management Guidelines for Healthcare Professionals

## General information

- Germline pathogenic variants (GPV - including class 4 likely pathogenic and class 5 pathogenic variants) in the **BMPR1A** gene cause juvenile polyposis syndrome (JPS).
- JPS refers to the histological type of poly,p not the age at which patients present. The classical juvenile polyp has a distinctive cystic architecture, dilated mucous filled glands and prominent lamina propria and Paneth cells within a dense infiltration of inflammatory cells.
- Clinical diagnosis of JPS requires:
  - a) >5 juvenile polyps in colon or rectum or
  - b) Juvenile polyps in other parts of the GI tract or
  - c) GPV in either **SMAD4** or **BMPR1A**.
- **BMPR1A** GPV may give a varied clinical picture including juvenile polyps, adenomas and hyperplastic polyps.
- **BMPR1A** GPV are present in 25-30% patients with JPS.
- Individuals with contiguous gene deletions of **BMPR1A** and **PTEN** have been described. These patients should be managed for both PTEN-HTS and JPS.
- Large deletions of 10q23 are associated with juvenile polyposis of infancy.

## Associated risks

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
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<tbody>
<tr>
<td>Colorectal cancer</td>
<td>- Ill-defined in <strong>BMPR1A.</strong> Only small series published. Risk is lower than with <strong>SMAD4</strong> GPV carriers but can be up to 60%, although this is likely to be an overestimate due to biased ascertainment. - Median age of diagnosis 44 years.</td>
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<tr>
<td>Gastric cancer</td>
<td>- Risk unlikely to be significantly increased. Around 20% carriers will develop gastric polyps but malignancy has not been reported.</td>
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## Management recommendations

- Patients with **BMPR1A** pathogenic variants should be managed in collaboration with a centre of excellence within the Rare Disease Collaborative Network (RDCN) for Inherited Polyposes. For further information see [https://www.ukcgg.org/information-education/rare-disease-collaborative-networks/](https://www.ukcgg.org/information-education/rare-disease-collaborative-networks/)

### Surveillance

- **Colorectal:** Colonoscopic surveillance from age 15 (earlier if symptomatic). Intervals 1-3 yearly depending on colorectal phenotype.
- **Upper GI:** Upper GI endoscopy from 25 years (earlier if symptomatic). Intervals 1-3 yearly depending on upper GI phenotype.

### Family matters

- Refer to clinical genetics to facilitate genetic testing in at-risk family members. This is usually suggested around the age at which screening commences.
- Refer to clinical genetics for discussions on reproductive options.

## References

- Monahan et al. Guidelines for the management of hereditary colorectal cancer from the British Society of Gastroenterology (BSG), Association of coloproctology of Great Britain and Ireland (ACPGBI) and United Kingdom Cancer Genetics Group (UKCGG). Gut 2020;69:411-444
- Blatter et al. Disease expression in juvenile polyposis syndrome: a retrospective survey on a cohort of 221 European patients and comparison with a literature derived cohort of 473 SMAD4/BMPR1A pathogenic variant carriers. Genetics in Medicine 2020;22:1524-1532

## Patient resources