

Management Guidelines for *PMS2* Mutation Carriers

| Male <i>PMS2</i> approximate risks* | | | Female <i>PMS2</i> approximate risks* | | |
|-------------------------------------|---|--------------------------|---------------------------------------|---|--------------------------|
| Cancer type | <i>PMS2</i> mutation carrier (up to 80) | Population lifetime risk | Cancer type | <i>PMS2</i> mutation carrier (up to 80) | Population lifetime risk |
| Colorectal | 13% | 7% | Colorectal | 12% | 6% |
| Endometrial | - | - | Endometrial | 13% | 3% |
| Ovarian | - | - | Ovarian | Similar to population | 2% |
| Upper gastrointestinal | Similar to population | 5% | Upper gastrointestinal | Similar to population | 4% |
| Ureter/kidney | Similar to population | 3% | Ureter/kidney | Similar to population | 2% |
| Urinary Bladder | Similar to population | 2% | Urinary Bladder | Similar to population | <1% |
| Brain | Similar to population | <1% | Brain | Similar to population | <1% |
| Prostate | Similar to population | 18% | Prostate | - | - |

Approximate *PMS2*- age-dependent cumulative cancer risks*

| Current age | Male colorectal | Female colorectal | Endometrial |
|-------------|-----------------|-------------------|-------------|
| 30 | <1% | <1% | <1% |
| 40 | <1% | <1% | <1% |
| 50 | 2% | 2% | 1% |
| 60 | 4% | 3% | 4% |
| 70 | 7% | 6% | 9% |
| 80 | 13% | 12% | 13% |

Management recommendations*

- 1 Screening**
 - **Colorectal screening:** 2-yrly colonoscopy from age 35 to 75 -review at 75
 - **Gastric screening:** Helicobacter pylori one-off screening from age 25
 - **Cervical screening:** As part of the NHS cervical screening programme
 - No additional cancer screening is currently recommended outside of a research setting; **symptom awareness** to be advised
- 2 Risk-reducing surgery**
 - Consider risk-reducing **hysterectomy ALONE**, once childbearing is complete, no earlier than age of 45 (risks and benefits to be discussed)
- 3 Chemoprevention**
 - Discuss pros and cons of **aspirin chemoprevention** from age 25 to 65 (GP to prescribe): 150mg OD if ≤70kg or 300mg OD if >70kg (**expert opinion**)
- 4 Research**
 - **Research studies:** e.g. **EUROPAC** (pancreatic cancer screening study)
- 5 Cancer management**
 - **Targeted therapies** may be available as a treatment option for certain cancer types (immune checkpoint inhibitors e.g. pembrolizumab)
 - **Adjuvant 5-FU chemotherapy** may not be appropriate for patients with Dukes' B colorectal cancers
- 6 Family matters**
 - Facilitate **cascade testing** in at-risk family members
 - Discuss **reproductive options**

*See FAQ document for further information: for questions or comments contact: Bianca.DeSouza@gstt.nhs.uk