

Management Guidelines for *MLH1* Mutation Carriers

Male <i>MLH1</i> approximate risks*			Female <i>MLH1</i> approximate risks*		
Cancer type	<i>MLH1</i> mutation carrier (up to 75)	Population lifetime risk	Cancer type	<i>MLH1</i> mutation carrier (up to 75)	Population lifetime risk
Colorectal	57%	7%	Colorectal	48%	6%
Endometrial	-	-	Endometrial	37%	3%
Ovarian	-	-	Ovarian	11%	2%
Upper gastrointestinal	22%	5%	Upper gastrointestinal	11%	4%
Ureter/kidney	5%	3%	Ureter/kidney	4%	2%
Urinary Bladder	7%	2%	Urinary Bladder	5%	<1%
Brain	<1%	<1%	Brain	2%	<1%
Prostate	Similar to population/ may be increased	18%	Prostate	-	-

Approximate *MLH1*- age-dependent cumulative cancer risks*

Current age	Male colorectal	Female colorectal	Endometrial	Ovarian
30	5%	0%	0%	0%
40	16%	12%	2%	2%
50	34%	21%	15%	6%
60	45%	32%	27%	10%
70	53%	44%	35%	11%
75	57%	48%	37%	11%

Management recommendations*

- 1 Screening**
 - **Colorectal screening:** 2-yrly colonoscopy from age 25 to 75—review at 75
 - **Gastric screening:** Helicobacter pylori one-off screening
 - **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**
 - Offer risk-reducing **hysterectomy with BSO**, once childbearing is complete, no earlier than age of 35- 40 (risks and benefits to be discussed)
 - HRT should be offered until age 51 in women who have not had a ER positive breast cancer
- 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. **IMPACT** (prostate cancer screening study) and **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)
 - **Surgical management of colon cancer:** discussion regarding pros and cons of segmental vs. extensive resection may be appropriate
 - **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