Yorkshire Cancer Research Bowel Cancer Improvement Programme
Lynch Syndrome and Aspirin Algorithm – v3.0 draft February 2023

Benefits of Aspirin for Patients with Lynch Syndrome:

- Lynch syndrome affects around one in 300 people in the population. Lynch Syndrome causes around 3% of bowel cancer cases.
- NICE recommends all patients with Lynch Syndrome be informed that taking aspirin reduces the chance of bowel cancer.
- The CAPP2 trial found for patients with Lynch syndrome, Aspirin 600mg daily, for an average of two and a half years, reduced the rate of bowel cancer by a third, prevention becomes apparent at 4 years and persists at 10 years. In numbers needed to treat terms, for 25 people treated there was 1 less person with cancer at 10 years.

Information to inform aspirin dosing decision making:

- Current efficacy data for aspirin applies to patients aged 65 and under.
- The older the patient is, the more likely they are to get side effects.
- Patients with Lynch syndrome may be pregnant or breast feeding. There should be a discussion with the patient about dosage of aspirin, risk and benefits to enable informed decision-making (see slide 2).

Useful Links:

Guidelines Recommending Aspirin Therapy in Lynch Syndrome

1. NICE 2020 - Patient Decision Aid - Lynch Syndrome: taking aspirin to reduce the chance of bowel cancer
2. NICE Guidance 2017 - DG27 Molecular testing strategies for Lynch syndrome in people with colorectal cancer (Point 2.13)
3. European guidelines from the EHTG and ESCP for Lynch syndrome: updated 3rd edition of the Mallorca guidelines based on gene and gender (pg 494)
4. NICE performed an 'exceptional surveillance' supporting NG151 in August 2020 2020 exceptional surveillance of colorectal cancer (NICE guideline NG151)
5. The International Aspirin Foundation website has a section on guidelines for prescribing aspirin https://www.aspirin-foundation.com/
6. Online Training for primary care clinicians Lynch Syndrome online training for primary care clinicians
7. UK Cancer Genetics Group One-page Gene-Specific Management Guidelines

Trial Showing Benefit of Aspirin Therapy In Lynch Syndrome

1. Cancer prevention with aspirin in hereditary colorectal cancer (Lynch syndrome), 10-year follow-up and registry-based 20-year data in the CAPP2 study: a double-blind, randomised, placebo-controlled trial
2. Long-term effect of aspirin on cancer risk in carriers of hereditary colorectal cancer: an analysis from the CAPP2 randomised controlled trial

Related studies exploring use of Aspirin in colorectal cancer or other approaches to reduce cancer risk in Lynch Syndrome

1. ADD-ASPIRIN: A phase III, double-blind, placebo controlled, randomised trial assessing the effects of aspirin on disease recurrence and survival after primary therapy in common non-metastatic solid tumours
2. Long-term effect of resistant starch on cancer risk in carriers of hereditary colorectal cancer: an analysis from the CAPP2 randomised controlled trial

Patient Resources

- Lynch Syndrome UK.

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The SNOMED codes for Lynch Syndrome are:
716318002 - Concept ID
33055050110 - Description ID

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Step by step approach to the use of aspirin in Lynch Syndrome

Is the patient suitable ?

- For patients diagnosed with Lynch syndrome:
- If your patient is currently receiving treatment for colorectal cancer you should wait until that treatment has been completed until prescribing aspirin
- Prescribe aspirin in accordance with Standard Product Characteristics (SPC)
- Patient should be between the ages of 18 and 70

Is the patient at risk from taking aspirin?

- Your patient should not be prescribed aspirin if they allergic or intolerant to it.
- You should discuss the pros and cons of taking aspirin with your patient (include information about dose and duration)
- Patient should not take aspirin if:
  - they are frail or suffer poor health such that it is judged the possible benefits are outweighed by risk of side effects
  - they are taking anticoagulating or antiplatelet medicines (other than aspirin)
  - they have uncontrolled hypertension
  - they have previously suffered from an aspirin or NSAID induced gastrointestinal bleed
  - NICE guidance and the SpC confirm lower doses of aspirin are safe in pregnancy but not recommended if breast feeding. Do not use the standard dose of 300mg for Lynch chemoprevention, if continuing using aspirin, please use 75mg and stop using it completely in the third trimester and if breastfeeding

Are they Helicobacter pylori negative?

- Aspirin induced gastrointestinal bleeding is less common in those who are Helicobacter pylori negative
- Please ensure your patient is H. pylori negative before starting aspirin;
  - Review result of previous test (if tested as part of cancer treatment)
  - Or, test within local guidelines (faecal, breath or serological)
- If patient is positive, they will need to receive H. Pylori eradication therapy before starting aspirin therapy

Initial aspirin dose

- Prescribe 75mg aspirin daily for 8 weeks (run-in period)
- If your patient experiences any side effects then they should stop it immediately and make an appointment for review and discussion of options

Ongoing aspirin prescribing?

Patient has tolerated the aspirin over the run-in period with no side effects:

- The CAPP2 trial dosed aspirin at 600 daily and reported no increase in adverse events compared to placebo. The population was relatively young. Other data raise concern for increased risk at lower body weight (Rothwell et al.) and at older age. The evidence base does not provide information on the aspirin dose that will optimally balance the benefit against risks of gastrointestinal bleeding. The CaPP3 trial is comparing different doses of aspirin, will report in 2025 and is being monitored by NICE.
- A lower dose is recommended by the UK Cancer Gene Group guidelines for all patients (300mg) with a body weight above 70kg. Reduce in those with a body weight below 70kg (150mg)
- If aspirin is tolerated, continue until age 60 and then review. Use beyond 70 years of age should be discussed with the patient as there is no evidence to use beyond this age. If there is emerging frailty or other life limiting comorbidity, stop aspirin.
- Review as part of GP annual medication review

Patients who do not tolerate the aspirin:

- Discuss possible options with the patient and consider:
  - Stopping aspirin completely (recommended if bleeding complication)
  - Re-try aspirin with a PPI and/ or at a lower dose