FULL PROTOCOL TITLE

ASCOLT: Aspirin for Dukes C and High Risk Dukes B Colorectal Cancers - An International, Multi-centre, Double Blind, Randomised Placebo Controlled Phase III Trial

STUDY CHAIRS

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LINK TO STUDY

https://gicancer.org.au/clinical-trial/ascolt/

TRIAL IDENTIFIER

ACTRN12614000513617

COORDINATING CENTRES

NHMRC Clinical Trials Centre (ANZ)

National Cancer Centre Singapore (International)

FUNDING SOURCES

Cancer Australia

PRESENTER

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FINANCIAL DISCLOSURE

None to declare.

AIM/S

To assess the effectiveness of aspirin against placebo control in patients with Dukes C or high risk Dukes B colorectal cancer in terms of Disease Free Survival (DFS) and Overall Survival (OS). The primary endpoint is DFS, with secondary objectives including OS at 5 years, DFS and OS in different ethnic groups, cancer sub-groups and compliant versus non-compliant patients.

BACKGROUND

Aspirin is a cost-effective and familiar medication. Evidence is emerging that it has anticancer properties, particularly in gastrointestinal cancers. Indirect evidence from five meta-analyses of randomised trials in patients with vascular disease showed that long term use of aspirin reduces the primary incidence of colorectal cancer (CRC) by about 40-50%. Randomised trials performed in patients at high risk for CRC reported that aspirin can reduce the development of polyps (the precursors of CRC) as well as the incidence of CRC. Although several cohort studies have suggested that aspirin improves survival in patients with localised CRC, prospective evaluation of the benefit of aspirin as an adjuvant agent in patients with a history of CRC has yet to be conducted.

The ASCOLT study is an international randomised phase III trial investigating the effect of aspirin as additional adjuvant treatment on disease free survival and overall survival in patients with resected stage II and III CRC. It is testing a critical question aimed at improving the survival of patients with potentially curable high risk localised colorectal cancer. The study is likely to have adequate power to identify subgroups that derive specific benefit from aspirin. It is hoped that aspirin may become a cost-effective personalised or targeted therapy.

STUDY DESIGN

ASCOLT is a multi-centre international Phase III trial in participants with stage III and high risk stage II colon cancer, stage II and III rectal cancer who have had resection of their primary tumour and have completed standard adjuvant therapy (chemotherapy ± radiotherapy). Participants are randomised to the study within 120 days of completion of adjuvant therapy in a 1:1 ratio to either:

- Aspirin arm: 200 mg aspirin once a day for 3 years
- Placebo arm: 200 mg matching placebo once a day for 3 years.

Participants have 3-monthly follow-up assessments for 3 years (months 3 to 36), followed by 6-monthly assessments for additional 2 years (months 42 to 60). Some participating sites offered an optional annual extended survival follow-up beyond 60 months, which concluded on 31 March 2023.

ELIGIBILITY CRITERIA

INCLUSION CRITERIA

- Adults (18 years or over) with high-risk stage II and III colorectal cancer (Dukes C colon cancer, high-risk Dukes B colon cancer, Dukes C rectal cancer, or Dukes B rectal cancer)
- Has undergone complete resection to remove the primary tumour
- Completed at least 3 months of chemotherapy, with or without radiotherapy

- Within 120 days of completion of standard therapy (surgery or chemotherapy with or without radiotherapy)
- Satisfactory haematological or biochemical functions (tests should be carried out within 8 weeks prior to randomisation)
- Willing to follow all study requirements, including treatment, timing of required assessments and follow-up.

EXCLUSION CRITERIA

- Pre-existing bowel diseases such as familial adenomatous polyposis, inflammatory bowel disease or ulcerative colitis
- Uncontrolled blood pressure
- Allergy to aspirin
- Patients taking a proton pump inhibitor (PPI) continuously for more than 1 year
- Active gastric or peptic ulcers, or gastro-intestinal bleeding within the past one year
- History of stroke, cardiovascular or vascular disease
- Patients already taking aspirin in the long term for other medical reasons.

STUDY UPDATE

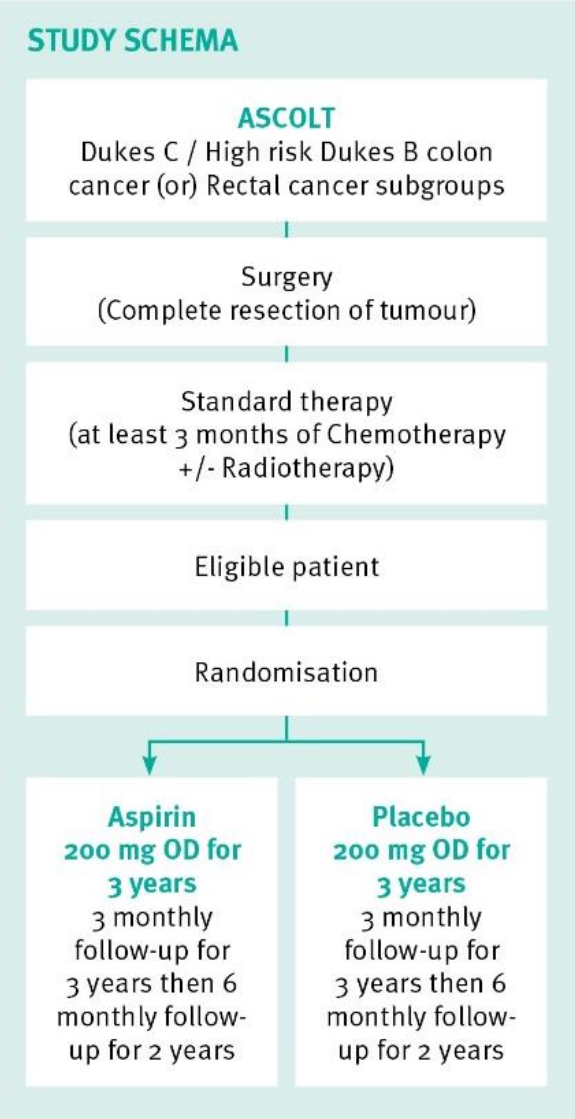
- ASCOLT is coordinated by the National Cancer Centre Singapore and is currently open in Singapore, Taiwan, Saudi Arabia, Malaysia, Indonesia, Hong Kong, China, India, South Korea, Australia and New Zealand. In ANZ, the trial is supported by Cancer Australia grant funding; having been awarded another grant in 2019.
- Target recruitment was reached on 30 June 2021, with ANZ site contributing 476 of the 1587 participants worldwide.
- Database lock for endpoint analysis was completed on 09 June 2023 and at the time of writing, data is being analysed.
- ANZ participants who were on study treatment or in follow-up will continue until completion of the protocol.

TRANSLATIONAL RESEARCH

In ANZ, archival tumour tissue and blood are collected at three time points from consenting participants: Baseline, six, and 12 months. Several countries in Asia including Singapore, Taiwan and Malaysia are also collecting biological samples.

The Australasian-led translational research in ASCOLT focuses on the predictive value of key biomarkers identified from retrospective studies, particularly tumour PIK3CA mutation and COX-2 overexpression. These samples will be a rich resource for other studies of CRC prognostic markers.

Analysis of tissue-based PIK3CA mutation and COX-2 expression is ongoing. Preliminary circulating tumour DNA (ctDNA) analysis of ANZ participants' samples has been conducted, with results presented at ESMO World GI 2022, ESMO 2022, and an abstract submitted for ESMO 2023.


STUDY SCHEMA
ASCOLT
Dukes C / High risk Dukes B colon cancer (or) Rectal cancer subgroups
Surgery
(Complete resection of tumour)
Standard therapy
(at least 3 months of Chemotherapy +/- Radiotherapy)
Eligible patient
Randomisation
Aspirin
200 mg OD for 3 years
3 monthly follow-up for 3 years then 6 monthly follow-up for 2 years
Placebo
200 mg OD for 3 years
3 monthly follow-up for 3 years then 6 monthly follow-up for 2 years