DYNAMIC-III Lay Summary

Title: Circulating Tumour DNA Analysis Informing Adjuvant Chemotherapy in Stage III Colon Cancer: A Multi-centre Phase II/III Randomised Controlled Study (DYNAMIC-III)

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Study Background and Rationale

Colorectal cancer is the second most common cancer in both males and females and the second most common cause of cancer-related deaths in Australia. Worldwide, around 250,000 patients are diagnosed with stage III colon cancer, that is, where the disease has spread beyond the bowel and into lymph glands.

Currently, the standard treatment for stage III colon cancer is surgical removal of the tumour followed by 3-6 months of chemotherapy. Chemotherapy is given as a combination treatment made up of 3 drugs including oxaliplatin or as a single drug treatment with fluoropyrimidine. Although studies have shown that chemotherapy reduces the risk of the cancer returning, not all patients benefit from treatment. For some, the cancer is cured by surgery alone, and others will experience cancer relapse even with treatment. It is difficult to adequately measure risk and treatment effectiveness for all patients.

The use of a biomarker that can better define the risk of the bowel cancer returning could make a major impact on treatment decisions for patients with stage III colon cancer. Circulating tumour DNA (ctDNA) may act as one such biomarker. For some people, cancer DNA can be found circulating in the bloodstream after the surgery to remove their bowel cancer, which provides evidence that some cancer cells have escaped and travelled to other parts of the body. A previous study in patients with bowel cancer has shown that people with ctDNA detected in their blood after surgery have a very high chance of the cancer coming back compared to those with no ctDNA. Therefore, this study is trying to see if a chemotherapy decision based on the presence (positive test) or absence (negative test) of ctDNA after surgery will be more effective at determining the optimal type and duration of chemotherapy treatment that a patient will need after surgery.

Study Aims

To demonstrate that a chemotherapy decision based on the presence or absence of circulating tumour DNA after surgery, will be more effective than standard of care treatment as measured by how many patients remain cancer free at 3 years.

Proposed study design

Patients will be randomised 1:1 to be treated according to ctDNA results after surgical removal of their bowel cancer or per standard of care. For the ctDNA –informed group, patients with a positive test will be treated with stronger chemotherapy than routine treatment. Patients with a negative test result will have milder chemotherapy or a shorter duration of routine treatment. Please see study schema on page 3.

Enrolment will be split (stratified) into separate groups based on the participating centre and clinical risk groups (low risk; high risk).

Proposed Recruitment and Follow-up

It is anticipated that 1000 eligible patients will be recruited over a 4.5-year period from approximately 20 Australian and international sites. All patients will be followed until death or study completion. The trial will be considered closed after the last patient enrolled has had 2 years of follow-up. It is anticipated that this study will run for approximately 6.5 years.

Study Restrictions

The study is restricted to patients 18 years and over. Patients with the following conditions will be excluded from the study:

- History of another primary cancer within the last 3 years, with the exception of non-melanomatous skin cancer and carcinoma in situ
- Patients with more than one primary colorectal cancers
- Patients treated with chemotherapy and/or radiation prior to surgery
- Patients with pre-existing Grade 2 peripheral neuropathy (sensory or motor)
- Patients with inadequate organ function
- Patients with significant cardiovascular disease
- Patient with medical or psychiatric condition or occupational responsibilities that may impact on compliance with the protocol

STUDY SCHEMA