PA12-15 Gerlinger Lay summary

Principal Investigator: Dr Marco Gerlinger, Clinical Lecturer at Barts Cancer Institute, London

Lay title:

Development of new blood based markers to measure drug effectiveness and to personalise treatment in prostate cancer patients.

What are you proposing?

Tumours release genetic material (DNA) into the blood which carries tumour specific alterations (mutations). This so called circulating tumour DNA (ctDNA) can be extracted and mutations can be detected by genetic sequencing technologies. Our aim is to count mutated ctDNA molecules in blood samples from patients with prostate cancer to answer two questions:

1. Are the changes in mutation counts in blood better markers of treatment response in prostate cancer patients than existing methods that assess treatment success?
2. Can blood based mutation detection identify patients which are unlikely to respond to certain treatments for prostate cancer such as abiraterone?

Why are you proposing it?

Prostate cancer frequently spreads into the bone (metastasis) which is difficult to assess with imaging techniques such as CT or bone scans. Thus, doctors usually rely on changes in the tumour marker prostate specific antigen (PSA) to check whether a new treatment is effective or not. PSA is the best test currently available but has many limitations. Thus, new techniques to assess treatment responses are an urgent clinical need. The latest DNA sequencing technology can be applied to blood samples to count mutated ctDNA fragments. Changes in the mutation count during treatment may more accurately reflect anti-tumour effects of new drugs than PSA testing.

This technology may improve the ability of researchers to test new treatments and could accelerate the development of new therapies for prostate cancer patients. Furthermore, the mutation profile of tumours can change over time and individual tumours may acquire mutations which cause resistance to certain drugs. Currently, a piece of tumour needs to be removed from a patient to check if such resistance mutations have developed. This is uncomfortable and associated with risks such as bleeding. We will test whether resistance mutations can be identified directly in ctDNA extracted from simple blood samples.

How are you proposing to do it?

Blood samples will be collected from 50 patients before and during treatment for advanced prostate cancer. Mutated ctDNA fragments extracted from blood will be counted on one of the most advanced DNA sequencing machines. Changes in these counts occurring during treatment will be compared to PSA changes and to tumour shrinkage on CT images in patients who have metastases outside the bone. If there is a good correlation, we will aim to develop this technology into a new test for treatment effectiveness that can be used in the clinic. We will also test whether we can detect mutations in the androgen receptor gene in ctDNA. Such mutations can cause drug resistance and we will assess whether patients with androgen receptor mutations in ctDNA have a poor response to the drug abiraterone. This test could tell doctors whether abiraterone is likely to be effective in an individual patient before treatment is started.

How long will it take?

Sample collection and analysis will be performed over a period of 12 months.

What is the budget?

£50,000

Why is this project suitable for a pilot award?

This new approach applies one of the most advanced genetic technologies to blood samples from prostate cancer patients to address an urgent clinical need. If successful, this is likely to have great impact on drug development and patient management, fulfilling the criteria for a pilot award.

What are the expected outcomes?

This project should reveal whether ctDNA testing is suitable to assess the effectiveness of drug treatments. This technology could accelerate the development of new treatments for prostate cancer. The detection of resistance mutations in ctDNA should allow treatment personalization without the need for more invasive techniques.

How could it make a difference to the lives of men affected by prostate cancer?

The technologies we’re developing could accelerate the development of new drug treatments for men with prostate cancer and may also allow the personalization of cancer treatment without the need to perform needle biopsies. Thus, patients could be spared side effects from a drug they are unlikely to benefit from.

Please write a summary of the project in one sentence only.

Our aim is the detection of genetic markers in the blood of patients with prostate cancer that help to assess whether a patient responds to a new drug and to determine which drugs are most likely to be beneficial in an individual patient.