Trial in Progress: Cancer Screening Study With or Without Low Dose Lung CT to Validate a Multi-cancer Early Detection Blood Test: SUMMIT

INTRODUCTION

Screening for breast, colorectal, and cervical cancers is recommended in the US, Canada, and most European countries, although guideline-recommended modalities, screening age range, and screening frequency vary substantially. Evidence for screening for lung cancer using low-dose computed tomography (LDCT) comes from the US National Lung Screening Trial of asymptomatic individuals with a substantial smoking history, which showed a 20% reduction in lung cancer mortality, and the Dutch Randomized NSRC trial, which reported CT screening reduced the risk of lung cancer-related deaths at 10 years by 26%. However, uptake of LDCT screening in the US has been very low due to barriers at the patient, physician, and healthcare system levels (eg, smoking stigma, fear of radiation, lack of awareness of screening guidelines among physicians and patients, and variable access).

A simple blood test that accurately detects cancer early and identifies its tissue of origin via measurement of tumor cell-free DNA (ctDNA) could reduce the number of false positive results and other potential harms associated with cancer screening, improve the patient experience, and improve patient outcomes.

METHODS

The SUMMIT Study is designed to validate the ability of a blood test to detect multiple cancer types among a high-risk population undergoing LDCT for lung cancer screening, as well as a lower risk population.

The SUMMIT Study will also examine the implementation of an LDCT screening service, including the following key study procedures:

- Enrolment of participants to Group A (individuals meeting USPSTF criteria for lung cancer screening or having a ≥1.3% risk of developing lung cancer in the next six year per PLCOm2012) and Group B (Individuals not meeting Group A criteria). At all visits, Group A participants also undergo LDCT at YO, Y1, and Y2.
- Participants will provide a blood sample and complete a questionnaire at three study appointments (baseline, 12 months post baseline, participants will provide a blood sample, complete a questionnaire, and if a current smoker, will receive a smoking cessation intervention.
- Participants will have a negative baseline LDCT (without lung nodules) will be randomised at their Year 1 visit to either have a follow-up scan or no scan.
- Participants with abnormal LDCT findings suspicion of cancer or other significant incidental findings will receive an urgent referral for diagnosis and treatment.

Eligibility criteria are as follows:

- Participants recruited will be asymptomatic adults between 50 and 79 years old who are current smokers or former smokers who quit within the past 15 years.
- Participants must also have a personal history of cancer, a family history of cancer, or a smoking-related condition.
- Participants with a negative baseline LDCT (without lung nodules) will be randomised at their Year 1 visit to either have a follow-up scan or no scan.
- Participants with abnormal LDCT findings suspicion of cancer or other significant incidental findings will receive an urgent referral for diagnosis and treatment.

Study Participants

- Participants will provide a blood sample, complete a questionnaire, and receive a baseline LDCT.
- Current smokers will receive a smoking cessation intervention.
- Measures of performance will include sensitivity, specificity, positive predictive value, and negative predictive value.

Study Objectives

- The primary objectives of the SUMMIT study are to:
  - Validate a cell-free nucleic acid blood test for detection of multiple cancers; and
  - Evaluate behavioral outcomes and participant acceptability associated with an LDCT screening programme.

Statistical Considerations

- The evaluation of the cfNA blood test performance will be performed using a nested case-control design: blood samples will be analysed from all participants who developed any type of cancer and a randomly selected subset of participants who did not.

- Measures of performance will include sensitivity, false-positive rate, specificity, positive predictive value, and negative predictive value.

- The evaluation of the implementation of an LDCT screening service, including participant experience, will be descriptive with summary results expressed as per 1000 screen or percentage.

CONCLUSIONS

- The SUMMIT Study is designed to determine the performance of this investigational multi-cancer blood test compared to or combined with LDCT for identifying lung cancer, and in detecting cancers for which there are no effective screening tests.
- The SUMMIT Study will evaluate the implementation of an LDCT screening programme in the London population.
- The SUMMIT Study may therefore inform new approaches to finding cancer early.

REFERENCES