Cologuard® for colorectal cancer screening

TECHNOLOGY

Cologuard®, is a multi-target stool screening test for colorectal cancer and advanced pre-malignant lesions, developed by Exact Sciences Corporation. It is intended for use as a screening test through the detection of mutated or altered DNA known to be associated with colorectal neoplasia or faecal haemoglobin. Cologuard® is intended for adults of either sex aged 50 years or older, who are at average risk of colorectal cancer (CRC).

Cologuard® utilises a multi-target approach to detect DNA and haemoglobin biomarkers associated with CRC or pre-cancerous cells, which are shed in a patient’s stool sample. Three independent categories of biomarkers are targeted: aberrant DNA methylation; DNA point mutations in the KRAS gene (which have been detected in up to 35% of CRCs); and non-DNA based biomarkers associated with colonic bleeding such as haemoglobin.

Stool samples are collected using the Cologuard® collection kit, which includes a protein sample tube with stool collection stick and buffer, a stool collection container, a foldable plastic bracket, a liquid DNA preservative buffer and a mailing container. At the laboratory, the targeted DNA is amplified and analysed for molecular alterations associated with cancerous and pre-cancerous conditions of the colon or rectum. Results from the methylation, mutation and haemoglobin assays are then combined in an algorithm to determine a positive or negative reportable result. To ensure the integrity of the sample, the laboratory must begin processing a specimen within 72 hours of collection.

The company is planning to apply for CE marking later this year, with launch for NHS clinical use anticipated before the end of 2014.
POTENTIAL FOR IMPACT

CRC (also known as bowel cancer) is the third most common cancer and is the second leading cause of cancer deaths in the UK. The majority of CRCs develop from initially benign adenomatous polyps in the bowel wall. A series of genetic alterations usually results in the transformation of normal epithelium to a precursor adenoma and then ultimately to carcinoma. The disease progresses slowly and takes approximately ten years for an adenoma to develop into cancer. This long latency period provides an opportunity for early detection of the disease at multiple points in time during a periodic programme of screening.

Screening for CRC can be carried out by bowel visualisation techniques (e.g. colonoscopy) and tests that measure biomarkers such as occult blood and DNA in a sample of faeces, blood or tumour tissues. The National Health Service Bowel Screening Programme offers screening every two years to all men and women aged 60 to 69, with the aim of detecting bowel cancer at an early stage, when treatment is more likely to be effective.

The company claims that Cologuard® is not intended as a replacement for diagnostic colonoscopy. Cologuard® shares some of the beneficial features of the currently used faecal occult blood test and faecal immunochemical test, such as non-invasiveness and use of sample collection devices containing liquid buffer. The added benefit of Cologuard® is that because cellular exfoliation of DNA into stool occurs continuously, the company claim this test can detect pre-malignant cells at early onset of abnormality, and with increased sensitivity for colorectal cancer and pre-malignant lesions. However, this test still requires faecal handling and poor compliance with stool-based tests is a barrier to CRC screening.

If proven to be effective, Cologuard® may offer the NHS an alternative non-invasive screening test for the early detection of CRC and faecal haemoglobin.

EVIDENCE

PUBLISHED PAPERS AND ABSTRACTS


COMPLETE UNPUBLISHED STUDIES

No complete, unpublished studies of this test were identified for this alert.

COMPANY INFORMATION

Further references for Cologuard® can be found at: http://www.exactsciences.com/solution/scientificreferences/

Two prospective studies and one case-control study are ongoing.

INFORMATION FROM

This Alert is based on information from the company and a time-limited internet search.