

HTG EdgeSeq ALKPlus Assay EU for ALK status testing in non-small-cell lung cancer

Medtech innovation briefing

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Summary

- The technology described in this briefing is HTG EdgeSeq ALKPlus Assay EU. It is used to identify mRNA ALK gene fusion events in lung tumour specimens taken from people with non-small-cell lung cancer (NSCLC).
- The innovative aspects are that the test automatically generates a report on ALK status that any clinician can interpret.
- The intended place in therapy would be to replace current methods of ALK status testing in people with NSCLC.
- No publically available evidence was found about the use of the assay.
- Key uncertainties around the evidence or technology is the lack of evidence on its diagnostic accuracy. Studies which specifically assess its diagnostic accuracy and compare it with current methods of ALK status testing are essential.
- The cost of HTG EdgeSeq ALKPlus Assay EU is £250 to £300 per test (excluding VAT). The resource impact would be higher costs compared with current methods of ALK status testing.

The technology

HTG EdgeSeq ALKPlus Assay EU (HTG Molecular Diagnostics) is an in vitro diagnostic assay which is designed to identify the ALK status of NSCLC. It is a next-generation sequencing (NGS)-based

assay that works with the company's HTG EdgeSeq analyser. The test is only compatible with Illumina MiSeq and MiSeqDx systems. The test is done on stored formalin-fixed, paraffin-embedded (FFPE) lung tumour specimens.

Innovations

The test differs from current methods of ALK status testing in that it automatically generates a report on ALK status. The report is presented in a way that needs no special training or experience to understand.

Current NHS pathway or current care pathway

The NICE guideline on [lung cancer](#) recommends that ALK status testing should be done for all people with non-squamous NSCLC at diagnosis, because the mutation is more common in this subgroup.

ALK status testing is done through fluorescence in situ hybridisation (FISH), immunohistochemistry, chromogenic in situ hybridisation and reverse transcription polymerase chain reaction (RT-PCR).

Population, setting and intended user

HTG EdgeSeq ALKPlus Assay EU would be used in secondary or tertiary care clinical laboratories and run by qualified laboratory staff with appropriate training.

People with non-squamous NSCLC are most likely to have ALK fusions, as well as people with squamous NSCLC that show the characteristics of being ALK positive (for example, younger people or those who don't smoke). The company estimates that approximately 50,000 people have ALK status testing each year.

Costs

Technology costs

The company states that each test with HTG EdgeSeq ALKPlus Assay EU costs £250 to £300. Upkeep of the HTG EdgeSeq analyser costs about £10,000 per year. Most laboratories will also need to purchase a compatible Illumina MiSeq or MiSeqDx system.

Costs of standard care

FISH testing costs £100 to £150 per test and takes 10 to 30 minutes. IHC testing costs £30 to 50 per test and takes around 2 minutes.

Resource consequences

HTG EdgeSeq ALKPlus Assay EU is not widely used in UK practice.

It can only be used with both an HTG EdgeSeq system and compatible Illumina MiSeq or MiSeqDx analyser. Specialist commentators estimate that around 25% of centres that test ALK status will have access to a MiSeq or MiSeqDx analyser.

The test produces a report which can be interpreted by any clinician, not just trained specialists.

Regulatory information

HTG EdgeSeq ALKPlus Assay EU was CE marked as a class III in vitro diagnostic device in March 2017. The HTG EdgeSeq system and Illumina MiSeq and MiSeqDx analysers are CE marked separately.

Equality considerations

NICE is committed to promoting equality, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. In producing guidance and advice, NICE aims to comply fully with all legal obligations to: promote race and disability equality and equality of opportunity between men and women, eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, marriage and civil partnership, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief (these are protected characteristics under the Equality Act 2010).

No equality issues were identified. People with cancer are considered to have a disability and are protected under the Equality Act from the point of diagnosis.

Clinical and technical evidence

A literature search was carried out for this briefing which includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology.

Published evidence

No publicly available evidence was found about the use of HTG EdgeSeq ALKPlus Assay EU.

Overall assessment of the evidence

No ongoing or in-development trials were identified from a search of clinical trial databases. Comparative studies would be useful to show how the test's diagnostic accuracy compares with other methods of ALK status testing.

Specialist commentator comments

Comments on this technology were invited from experts working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

All 3 specialist commentators were familiar with or had used the test before.

Level of innovation

All 3 commentators thought that the test was novel. One noted that it was differentiated from other methods of ALK status testing through the patient report and hands-off approach. Another specialist noted that minimal lung tissue (that is, stored FFPE specimens) was needed for testing.

Potential patient impact

One commentator noted that HTG EdgeSeq ALKPlus Assay EU represents testing closer to the point of care than other methods of ALK status testing. Another felt that the assay could help standardise ALK status testing, and pointed out that it does not need another lung biopsy to be done. In contrast the third commentator felt that the test did not offer any advantages over other methods of testing.

One specialist commentator noted that once a MiSeq system is procured, it can be used in many pathways. Another stated that this test might have a higher detection rate than FISH, but that this is unlikely to be the case with IHC. One commentator felt that the test could lead to more accurate prediction of response to crizotinib, but another stated that there was no evidence to predict any potential impact.

Potential system impact

One commentator stated that ALK status testing is already adequate in practice. They noted that there may be cost savings through less reporting consultant time, but that any savings would be small compared with the increased cost per test. Another specialist observed that the test's reproducibility could benefit the NHS, as well as its reduced need for interpretation. One commentator noted that using the test would mean more sample transfers between testing centres, because not every centre has its own machine. Two specialist commentators agreed that the test would be cost incurring for the NHS.

General comments

Two commentators noted that next-generation sequencing (such as that done by HTG EdgeSeq ALKPlus Assay EU) generates a large amount of data, which may represent a substantial IT service commitment for data storage and maintenance.

One specialist noted that the research-use-only full patient report of multiple mutations may be useful if it can be validated internally by laboratories.

Specialist commentators

The following specialist commentators contributed to this briefing:

- Dr Sharon Barrans, clinical scientist, Leeds Teaching Hospitals NHS Trust. No relevant conflicts of interest.
- Dr Paul Cane, consultant histopathologist, Guy's and St Thomas' NHS Foundation Trust. No relevant conflicts of interest.
- Dr Alistair Reid, consultant clinical scientist, Liverpool Clinical Laboratories. No relevant conflicts of interest.

Development of this briefing

This briefing was developed by NICE in accordance with published [process and methods](#).

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