NICE advice

PredictSURE IBD for inflammatory bowel disease prognosis: ulcerative colitis

Medtech innovation briefing
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This advice replaces MIB178.

Summary

- This **briefing** covers the use of PredictSURE IBD for ulcerative colitis. NICE has also published diagnostics guidance on the use of PredictSURE IBD to guide treating Crohn's disease.
- The **technology** described in this briefing is PredictSURE IBD. It is a prognostic assay that categorises people with newly diagnosed inflammatory bowel disease (IBD) into a high or low risk of severe, inflammation of ulcerative colitis.
- The **innovative aspect** is that it is designed to help personalise treatment for people with ulcerative colitis who might benefit from early treatment with biologics.

- The intended **place in therapy** would be to help the gastroenterologist choose treatment for people diagnosed with ulcerative colitis.
- The **main points from the evidence** summarised in this briefing are from 2 studies including 1 prospective cohort study and 1 observational study with a total of 89 people with diagnosed ulcerative colitis in the UK. They provide proof of principle evidence that PredictSURE IBD could predict prognosis in people with ulcerative colitis.
- **Key uncertainties** around the evidence or technology are that limited evidence is available on the prognostic accuracy of PredictSURE IBD in people with ulcerative colitis. There was no evidence on how using PredictSURE IBD influences treatment decisions when managing active IBD.
- **Experts advised** that PredictSURE IBD may be a helpful test to determine the most appropriate treatment for people with ulcerative colitis; however, there is limited evidence to support that.
- The **cost** of PredictSURE IBD is £1,250 per person (excluding VAT). This includes the costs of the technology and the laboratory services.

The technology

PredictSURE IBD (PredictImmune) is a prognostic assay that predicts long-term disease outcomes in inflammatory bowel disease (IBD) such as ulcerative colitis. It stratifies people with IBD into a high or low risk of severe, relapsing inflammation of disease by detecting CD8+ (cluster of differentiation 8) T-cell exhaustion. The level of gene expression indicating CD8+ T-cell exhaustion is linked to disease course in multiple autoimmune diseases, including IBD. The test needs 2.5 ml of whole blood, which is processed in a reverse transcriptase polymerase chain reaction (RT-PCR). The test is run on a Roche LightCycler PCR platform. After measuring the expression of 17 genes, the company's algorithm produces a clinical outcome prediction (high or low risk) for severe, relapsing inflammation of ulcerative colitis.

Innovations

PredictSURE IBD is designed to help personalise treatment for people with ulcerative colitis. By identifying whose disease is more likely to progress to a severe and relapsing

inflammation, it may allow more personalised treatment.

Current care pathway

After initial diagnostic investigations and tests for IBD, investigations should assess the level of disease activity and the risk of long-term complications.

Disease activity for ulcerative colitis can be assessed using the:

- Simple Colitis Clinical Activity Index (SCCAI)
- Ulcerative Colitis Disease Activity Index.

Ulcerative colitis should be managed differently depending on the severity of disease. For mild to moderative disease, a topical aminosalicylate is recommended as a first-line treatment. For severely active ulcerative colitis, biologics and Janus kinase inhibitors are recommended.

The following publications have been identified as relevant to this care pathway:

- NICE guideline on ulcerative colitis: management
- ECCO-ESGAR guideline for diagnostic assessment in IBD part 2: IBD scores and general principles and technical aspects.

Population, setting and intended user

PredictSURE IBD is intended to be used in adults (16 years or older) with ulcerative colitis, who have active disease and are not receiving concomitant treatment such as steroids, immunomodulators or biologic therapies.

The test can be carried out in both inpatient and outpatient gastroenterology clinics and should only be used for people in an active flare of disease who are not on immunomodulatory medications. The blood sample needs to be taken by a trained professional (such as a phlebotomist, nurse or doctor). The sample is then processed by a centralised laboratory facility in Cambridge, and the result is returned to a specialist gastroenterologist normally within 7 days.

No additional staff training is needed to do the test, which is on an industry-standard LightCycler RT-PCR system.

Costs

Technology costs

PredictSURE IBD was launched in February 2019 and has been available for research use as a testing service only. The cost of the technology is £1,250 per person.

Costs of standard care

There is no standard testing currently in the NHS to personalise ulcerative colitis treatment. Current practice involves titrating and increasing drug treatment from steroids to immunosuppressives. Biological therapies are used on a 'step-up' and trial and error basis.

Resource consequences

Introducing PredictSURE IBD to the treatment pathway could lead to cost savings if starting treatment earlier results in reductions in disease flare-ups, use of maintenance treatment, surgery, disease complications and treatment complications.

The resource consequences of introducing the technology are low because the test uses existing technology and takes 2 to 7 days. This fits within the current NHS approach to treatment.

Regulatory information

PredictSURE IBD is a CE-marked in vitro diagnostic kit for use in certified clinical diagnostic laboratories. An application to include the PredictSURE IBD test within its UKAS ISO 15189 accreditation is expected to be submitted in Q4 2022.

No manufacturer field safety notices or medical device alerts for this technology have been identified.

Equality considerations

NICE is committed to promoting equality, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

Inflammatory bowel disease is more likely to be diagnosed in people in their 20s, but it can occur at any age. It is more common in people of African-Caribbean family origin or European family origin, particularly those with Eastern European Jewish backgrounds. Ulcerative colitis is slightly more common in men. Age, sex and ethnicity are protected characteristics under the Equality Act 2010.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the interim process and methods statement for medtech innovation briefings. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

Two studies are summarised in this briefing. One study used the underlying signature for PredictSURE IBD and provided biochemical 'proof of concept' evidence for the signature underlying PredictSURE IBD (Lee et al. 2011). Biasci et al. (2019) is a prospective study of 123 people with inflammatory bowel disease (IBD), which examined the use of PredictSURE IBD in clinical practice.

The clinical evidence and its strengths and limitations are summarised in the overall assessment of the evidence.

Overall assessment of the evidence

Evidence on PredictSURE IBD for predicting ulcerative colitis prognosis is limited in quantity and quality. A prospective cohort study recruited patients with IBD using the PredictSURE IBD test to predict the flare-ups of IBD including ulcerative colitis from diagnosis (Biasci et al. 2019). The study described the use of the test in 3 cohorts

including 2 training cohorts and 1 validation cohort. The PredictSURE IBD test stratified 2 patient subgroups by disease severity. Estimates of prognostic accuracy were available for the validation cohort, and the sample study for the estimates was small.

Biasci et al. (2019)

Study size, design and location

A prospective cohort study of 123 people with IBD, including 57 people with ulcerative colitis in the UK.

Intervention and comparator

PredictSURE IBD; no comparator.

Key outcomes

In the validation cohorts, PredictSURE IBD stratified patients into 2 distinct subgroups irrespective of their underlying diagnosis:

- IBDhi patients (with a poor prognosis of IBD, equivalent to IBD1, T-cell exhaustion low)
- IBDlo patients (equivalent to IBD2, T-cell exhaustion high).

Results suggested that people who were classified as IBDhi had significantly more aggressive diseases than those classified as IBDlo. The hazard ratio for an earlier need for treatment escalation in ulcerative colitis was 3.12 (95% confidence interval [CI] 1.25 to 7.72; p=0.015). The sensitivity and specificity for predicting the need for multiple escalations within the first 18 months were 100% and 48% in people with ulcerative colitis.

Strengths and limitations

This study also included 66 people with Crohn's disease. People included in the study had introduction treatment, which would likely influence the timing and frequency of subsequent escalations, and consequently sensitivity and specificity. The calculation of prognostic accuracy was based on a relatively small sample size.

Lee et al. (2011)

Study size, design and location

An observational prospective study of 32 people with ulcerative colitis in the UK.

Intervention and comparator

Standard care step-up strategy given by doctors blinded to the PredictSURE IBD signature test results (note – this study did not use the actual test but did use the same signature that is used in PredictSURE IBD). No comparator.

Key outcomes

The study used statistical techniques to identify 2 subgroups of patients, IBD1 (characterised by upregulation of the majority of differentially expressed genes) and IBD2. This showed CD8+ T-cell transcriptional signatures that identified 2 subgroups that had very different disease courses. Patients in the subgroup with elevated expression of genes involved in antigen-dependent T-cell responses had a substantially higher incidence of frequently relapsing disease. The authors comment that this suggests that the course of otherwise distinct autoimmune and inflammatory conditions may be influenced by common pathways and identifies the biomarker that can predict prognosis in ulcerative colitis.

Strengths and limitations

This study also included 35 people with Crohn's disease. The patients were recruited specifically for this study and all treatment was blinded to the test results. The study is relatively small and gives basic demographic information for the patients. Detailed descriptions of the treatment course and outcomes are presented in the supplementary information as are details of the complex statistical methods used in the analysis.

Sustainability

This is a single-use technology. The company states that it works with suppliers including raw material manufacturers with sustainability plans focusing on reducing carbon emissions, rethinking packaging, plastics recycling and responsible water usage. It also

works with its logistics partner to develop sustainable shipping to reduce CO_2 emissions. There is no published evidence to support these claims.

Recent and ongoing studies

- PRECIOUS Study: Predicting Crohn's and colitis outcomes in the United States. ClinicalTrials.gov identifier: NCT03952364. Status: recruiting. Indication: inflammatory bowel diseases. Devices: PredictSURE IBD. Date last updated: October 2021. US.

Expert comments

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

Three experts were familiar with or had used this technology before.

Level of innovation

All 3 experts agreed PredictSURE IBD was a novel technology. One said it was designed to enable people with inflammatory bowel disease (IBD) to have improved prognosis. They added that in theory, patients could be treated empirically based on the results of the test if it was shown to be robust and accurate. The other 2 experts said that the safety and efficacy of the technology remained uncertain because of the limited evidence base.

Potential patient impact

All 3 experts agreed that PredictSURE IBD could benefit people with IBD, including ulcerative colitis. They said that PredictSURE IBD could help determine the most appropriate treatment, and reduce the risk of relapse, by identifying who had a high likelihood of a severe, relapsing flare-up and offering them maintenance treatment. They said that everyone with active IBD would benefit from this technology. One expert noted that this could be particularly important to people with severe inflammation and may help avoid surgery and long-term complications.

Potential system impact

All 3 experts agreed that PredictSURE IBD could help clinicians decide on treatment for individual people. One noted that there was potential for this to reduce the length of hospital stays, surgery and long-term complications. However, this is highly dependent on the positive predictive value of the test, which has not yet been determined. Two experts said that using PredictSURE IBD was likely to lead to cost savings.

General comments

Two experts said that the technology would be helpful as an addition to current care for managing IBD. One noted that the current evidence suggests that the test successfully predicts disease outcomes in the early stages. However, its value depends on the effectiveness of early intervention and how well it discriminates between good and poor outcomes.

Expert commentators

The following clinicians contributed to this briefing:

- Professor Mohammad Ilyas, professor of pathology, Faculty of Medicine and Health Sciences, University of Nottingham. Did not declare any interests.
- Dr Anjan Dhar, consultant gastroenterologist, County Durham and Darlington NHS Foundation Trust. Dr Dhar is the principal investigator for the PROFILE trial.
- Dr Robert Logan, consultant gastroenterologist, King's College Hospital NHS Foundation Trust. Did not declare any interests.

Development of this briefing

This briefing was developed by NICE. The interim process and methods statement for medtech innovation briefings set out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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