

Background to the study

PRECIOUS is an observational study investigating the ability of a prognostic biomarker to predict long-term outcomes in inflammatory bowel disease (IBD) in the US. It utilises the PredictSURE IBD™ biomarker to stratify patients at diagnosis into high and low- risk cohorts, based on their risk of subsequently experiencing a severe disease course, characterised by the requirement for multiple escalations in treatment due to frequently-relapsing or chronically-active disease. The biomarker was developed by researchers at Professor Ken Smith's laboratory, at the University of Cambridge (UK); its discovery and validation has been presented at key conferences (including the Crohn's & Colitis Congress) and published in a number of prestigious peer-reviewed journals (McKinney et al 2010, Lee et al 2011, Biasci et al 2019). PredictImmune was founded in 2017 to commercialise the IBD biomarker test and successfully achieved a CE mark for the test in December 2018. The PredictSURE IBD™ test was launched in the UK as a kit in January 2019. PredictSURE IBD™ will form the basis of risk-stratification in the PRECIOUS study.

About the study

- Study design: A multi-center, observational study of patients with active Crohn's disease (CD) or ulcerative colitis (UC), who are not receiving systemic steroids, immunomodulators or biologics. The study will recruit up to 200 patients from centers across the US.
- Study aim: Assess whether a prognostic biomarker can stratify IBD patients in the US according to their subsequent disease course.
- Study duration: Recruitment will continue for 12 months, with follow up for up to 18 months following initial blood sample collection.
- Treatment algorithm: Patients will be treated using an accelerated step-up strategy in line with local practice.

Eligibility for the study

The target patient population is patients with active CD or UC, who are not currently receiving steroids, immunomodulator or anti-TNFα treatment/biologics. Patients are eligible if they meet the inclusion and exclusion criteria summarised below. Ideal patients for this study are newly diagnosed and treatment naïve.

Inclusion Criteria	Exclusion Criteria	Clinical Data to be Recorded
<ul style="list-style-type: none"> • Active UC or CD with typical symptoms in conjunction with at least one objective measure of disease activity: elevated CRP, calprotectin, endoscopic evidence. • Not currently receiving systemic therapy* with steroids, immunomodulators or biologics, and at least 7 days since the last steroid dose. • Due to be managed using a "step-up" or "accelerated step-up" approach (so will not receive biologics as first line therapy). • Aged 16-80 years old. 	<ul style="list-style-type: none"> • The presence of any of the following will preclude patient inclusion: • Patients with fistulating peri-anal Crohn's disease or active perianal sepsis. • Obstructive symptoms and evidence of a fixed stricture on radiology or colonoscopy. • Patients who are scheduled to start on "top-down" therapy or receive biologics as a first line therapy 	<ul style="list-style-type: none"> • Unique patient ID • Study entry date • Gender • Ethnicity & race • Date of birth • Smoking status • Disease location • Disease behaviour (Crohn's) • Perianal involvement (Crohn's) • CRP • Faecal calprotectin • Hemoglobin • Albumin • Harvey Bradshaw Index (Crohn's) • Modified Mayo score (UC) • Initial treatment • Date of treatment escalations (e.g. immunomodulators, biologics or surgery) and treatment received • Date of chart review • Other comments

*ideal patients for this study are newly diagnosed and treatment-naïve.

Study procedures & assessments

Newly diagnosed patients with CD and UC will be recruited from a predominantly outpatient setting. Potential study patients will be identified by local clinical team members and be given a patient information leaflet (PIL).

Assessments and data collection will be performed by appropriately trained and qualified research staff, as delegated by the principal investigator at each site.

Blood sample collection for biomarker risk assessment

A 2.5ml blood sample will be collected for the PredictSURE IBD™ test. The blood collection tubes and the boxes appropriate for the transport of biological material will be provided with the necessary pre-addressed slips. Once collected, the whole-blood RNA is stable for up to 48 hours at room temperature, so the boxes will need to be posted on the same day as the sample is collected.

Patient data collection/retrospective chart review

A spreadsheet or database will be provided to fill in the details about recruited patients, including a unique identifier. Data will be collected at the first visit (enrolment) with a retrospective patient chart review at end of study – up to 18 months after enrolment.

Informed consent

PredictImmune intends to engage with WIRB (<https://www.wirb.com/Pages/default.aspx>) to provide for a centralized IRB process.

Reimbursement

Reimbursement will be at the standard rate for such studies and is likely to be split into an up-front payment for enrolment of each patient and an end of study payment for each patient completing the study.

Data analysis

Previous studies have demonstrated the ability of PredictSURE IBD™ to stratify IBD patients into high- and low-risk of aggressive disease at the time of diagnosis. The aim of this study is to validate that PredictSURE IBD™ provides similar risk stratification in a US IBD population. As a consequence, data analysis will focus on looking for a correlation between risk category, as determined by the PredictSURE IBD™ test and clinical outcomes, as measured by the need for treatment escalation. Other clinical (endoscopy, HBI etc.) and laboratory (calprotectin, CRP levels) measures will also be evaluated. There will be a particular focus on the need for treatment escalations, time to first treatment escalation, number and frequency of treatment escalations as a measure of disease activity.

In partnership with:



For more information on the PRECIOUS study, please email: lardolli@predictimmune.com or khills@predictimmune.com
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(9am and 5pm GMT, Mon-Fri).

Bibliography

McKinney, E. (2010). A CD8+ T cell transcription signature predicts prognosis in autoimmune disease. *Nature Medicine*, 16(5), 586-592.
Lee, J. (2011). Gene expression profiling in CD8+ T cells predicts prognosis in patients with Crohn disease and ulcerative colitis. *JCI*, 121(10), 4170-4179.
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