

A blood-based prognostic biomarker in IBD: Towards personalised medicine

Introduction

There is a recognition that the management of inflammatory bowel disease (IBD) would benefit from a personalised approach where the choice of treatment is targeted to the individual patient. However, such a strategy requires the ability to predict disease course at diagnosis, an approach that is currently not possible. We have developed a whole blood-based qPCR prognostic test that stratifies patients with IBD (both Crohn's disease (CD) and ulcerative colitis (UC)) into two groups that correlate with clinical outcome^{1,2}.

Discovery and validation of PredictSURE IBD™

A machine learning approach utilising independent training (n = 69) and validation cohorts (n = 123) was used to develop a practical whole blood prognostic biomarker. The optimised qPCR-based model measures the expression of 15 informative and 2 reference genes. The model effectively

assigns the patients in the training group into high-risk (IBDhi) and low-risk (IBDlo) cohorts, consistent with the risk groups identified in our previously described CD8 discovery cohort (Lee et al 2011).

The prognostic test was then validated on an independent validation cohort of 123 IBD patients (66 CD, 57 UC). Patients were prospectively recruited at diagnosis from four UK hospitals and a risk group was assigned using the PredictSure™ assay. Development of the assay had been completed prior to this independent validation study. Patients were treated and followed up in accordance with national guidelines using a step-up strategy. Clinical follow up was reported by treating physicians blinded to the biomarker results using a predefined endpoint of treatment escalation (episodes of active disease requiring increased treatment or surgery).

Bibliography

1. Lee JC, et al. J Clin Invest 2011;121:4170-79
2. McKinney EF, et al. Nature 2015;523(7562):612-6

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Results

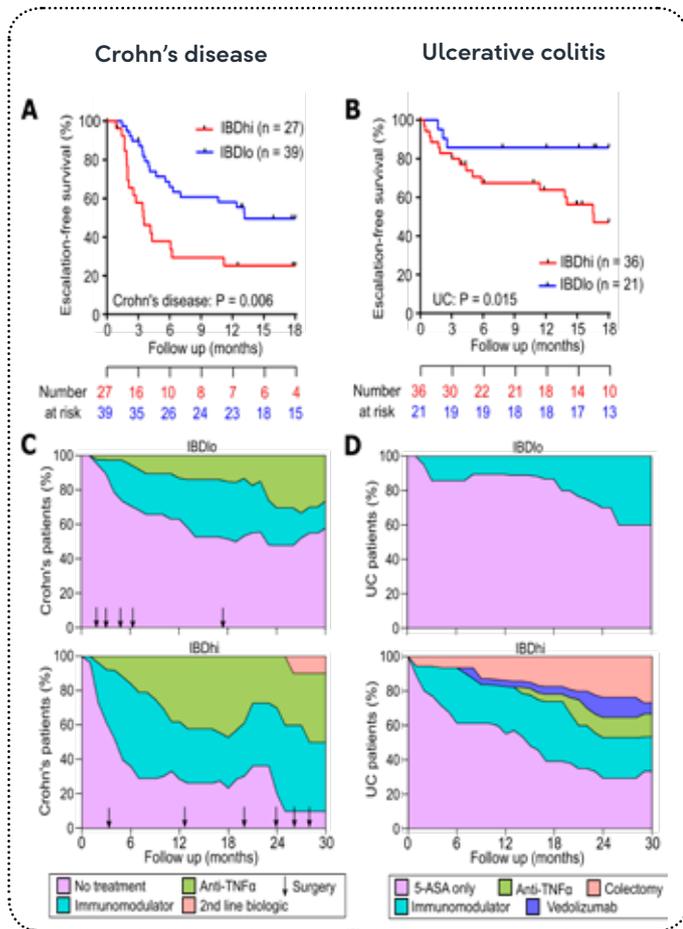


Figure 1. Validation of the qPCR-based classifier

Conclusions

We have developed a practical whole blood test that predicts, at diagnosis, clinical outcomes in patients with CD and UC. Patients assigned to the IBDhi and IBDlo risk groups experience very different disease courses. Patients in the IBDhi group have consistently more aggressive disease characterised by the

Clinical performance of the qPCR-based model was determined in an independent cohort of patients with active untreated CD or UC. Patients assigned to the high-risk group experienced a significantly more aggressive disease course characterised by:

- A shorter time to requiring a treatment escalation (hazard ratio (HR) 2.65 and 3.12 for CD and UC, respectively, Figure 1A-B).
- Increased risk of any treatment escalation (relative risk at 12m (RR) 1.7 and 2.8 for CD and UC respectively, Figure 1C-D).
- Increased risk of multiple treatment escalations (RR at 12m for IBD 17, RR 11 in CD, not determined in UC as no multiple escalations in low risk group).

need to escalate treatment earlier and more frequently than for patients in the IBDlo group. Specifically, 91% requiring multiple treatment escalations in the first 12 months were in the high risk group while 98% of the low risk group did not require them.

