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**Serum biomarkers predicting short-term and mid/long-term relapse in patients with Crohn’s disease stopping infliximab**

*Pierre N, Huynh-Thu V, Baiwir D, et al. External validation of serum biomarkers predicting short-term and mid/long-term relapse in patients with Crohn’s disease stopping infliximab. Gut 2024; 73: 1965-1973. doi: 10.1136/gutjnl-2024-332648.*

Infliximab withdrawal in patients with Crohn’s Disease (CD) in remission is often considered for various reasons. Around 50% of patients with CD in remission do not relapse over a 2-year period on stopping anti-TNF-α (tumour necrosis factor alpha). However, relapse remains unpredictable and the decision to withdraw can be difficult.

STORI (The study of infliximab diSconTinuation in CrOhn’s disease patients in stable Remission on combined therapy with Immunosuppressors) reported that in stopping infliximab in patients with CD the risk of short term (≤6 months) and mid/long-term relapse (>6 months) was associated with distinct blood protein profiles. The SPARE (A proSpective Randomized Controlled Trial comParing infliximAb-antimetabolites Combination Therapy to Anti-metabolites monotheRapy and Infliximab monothErapy in Crohn's Disease Patients in Sustained Steroid-free Remission on Combination Therapy) study is an open label randomised controlled trial where patients with CD in sustained steroid free clinical remission receiving combination therapy (infliximab and immunosuppressant) were allocated to 3 arms: continuing combination therapy, stopping infliximab or stopping immunosuppressant.

The aims of this study were to use the SPARE cohort to validate biomarkers highlighted in the STORI cohort. In the baseline serum of the STORI and SPARE(arm stopping infliximab) cohorts 202 immune related proteins were studied. The proteins associated with time to relapse were compared between the 2 studies.

In STORI and SPARE, distinct blood protein profiles were associated with the risk of short-term (e.g., high level: CRP (C-Reactive Protein), haptoglobin, interleukin-6, C-type lectin domain family 4 member C) and mid/long-term relapse (e.g., low level: Fms-related tyrosine kinase 3 ligand, kallistatin, fibroblast growth factor 2). At external validation, the top 10 biomarker pairs showed a higher c-statistic than the CEASE (previously validated) model, CRP and faecal calprotectin in predicting short-term (0.76–0.80 vs. 0.74 vs 0.71 vs. 0.69, respectively) and mid/long-term relapse (0.66–0.68 vs. 0.61 vs. 0.52 vs. 0.59, respectively).

Pierre *et al.,* identified some limitations to the study. The proportion of missing data was relatively high for faecal calprotectin. Also, the data on ethnicity was not collected and therefore this study cannot be generalised to other populations.

Pierre et al., concluded in patients with CD stopping infliximab, the risk of short-term and mid/long-term relapse is associated with distinct blood protein profiles showing the potential to guide infliximab withdrawal.