

Original Article

Exploration of Predictive Biomarkers of Early Infliximab Response in Acute Severe Colitis: A Prospective Pilot Study

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Abstract

Background: The outcomes of acute severe ulcerative colitis [ASUC] appear to be dependent on early intervention with the first and/or further infliximab [IFX] doses, although parameters to guide decision-making remain uncertain.

Aim: To assess whether serum/faecal IFX levels and inflammatory biomarkers early after IFX dose can predict ASUC outcomes.

Methods: This prospective pilot study consecutively recruited inpatients with steroid-refractory ASUC, who then received 1–3 IFX rescue doses [5 mg/kg per dose] at the discretion of the treating clinician. Serum IFX, C-reactive protein [CRP], albumin and faecal calprotectin [FC] concentrations were measured daily as an inpatient, and then 7, 14, 28 and 42 days post-first IFX. Faecal IFX was measured 1 day post-IFX. The primary end point was clinical remission (partial Mayo [PM] = 0) and CRP \leq 3 mg/l at 6 weeks. Secondary end points were 12-week clinical remission or colectomy during follow-up.

Results: Of 24 ASUC patients with a median follow-up of 28 months [range 13–44], 10 [42%] achieved remission at 6 weeks, 12 [50%] achieved 12-week remission, six [25%] had colectomy. In total, 97% received either two or three IFX doses. Post-first dose, receiver–operator curve-derived cutoffs of the area-under-curve [AUC, Days 4–7] concentrations for serum IFX, FC and PM scores each predicted the primary end point with 100% sensitivity, and predicted future colectomy with 89–94% sensitivity. In multivariate analyses, faecal IFX >1 μ g/g (odds ratio [OR] 0.04 [0.2, 0.9]), PM AUC_{d1-3} < 20 (OR 20.2 [1.01, 404], each $P < 0.05$), FC AUC_{d1-3} $< 10\,000$ μ g/ml [OR 13.6 [0.6, 294], trend only, $p = 0.09$) were each associated with clinical and CRP remission [6 weeks].

Conclusions: In ASUC, post-first dose IFX, early assessment of serum/faecal IFX, calprotectin and PM scores can accurately predict future remission and colectomy, and thus potentially aid in decision-making, i.e. accelerated IFX dosing or surgical planning if/when needed.

Key Words: Ulcerative colitis; infliximab; colectomy