

# Relationship between serum trough infliximab levels, serum antibodies to infliximab, serum albumin levels and clinical response to infliximab treatment in patients with inflammatory bowel diseases

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## Background

A better understanding of the relationship between serum infliximab trough levels (S-IFX) and disease characteristics may lead to more effective use of this treatment in inflammatory bowel disease (IBD) patients. S-IFX has a wide inter-individual variability. The objective of this study was to determine the possible association of infliximab disposition with the formation of serum antibodies to infliximab (S-ATI) and serum albumin levels (S-ALB).

## Patients and Methods

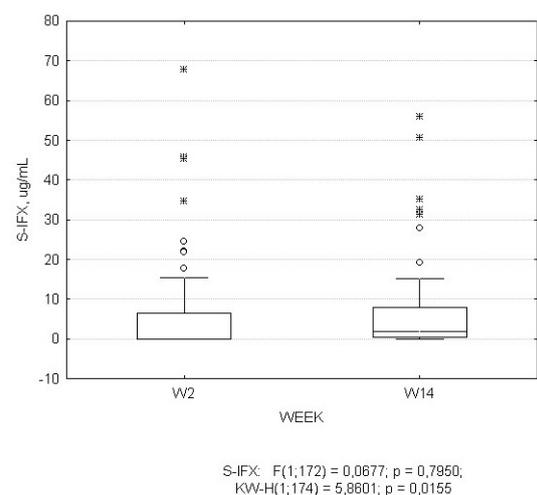
Eighty five patients with IBD receiving infliximab treatment were included in this retrospective study: 31 with ulcerative colitis (UC) and 54 with Crohn's disease (CD), 37 males and 48 females, with the mean age  $36 \pm 12$  years. All patients were given intravenous infusions of 5 mg/kg of infliximab at weeks 0, 2 and 6 during induction treatment regimen and after that, if response was achieved, maintenance therapy with the dose of 5 mg/kg was continued every other month. Sixty three patients (74 %) were evaluated as responders to the treatment, twelve patients (14 %) developed secondary non-response in the course of the treatment, and 10 (12 %) patients have experienced adverse effect of the treatment.

Serum samples of these individuals from the IBD blood bank from second (W2) and fourteenth (W14) week of treatment were assessed for S-IFX, S-ATI and S-ALB. Measurement of S-IFX and S-ATI were determined by enzyme linked immunosorbent assay (Matriks Biotek), albumin was detected by colorimetric BCG assay (Roche-Modular).

Different groups were compared by the Mann-Whitney U-test or a two-sided Kruskal-Wallis non-parametric test. The Spearman rank test was used for correlations between variables. The threshold for significance was set at  $p < 0.05$ .

## Results

S-IFX levels at W2 were significantly lower compared to W14 values ( $p = 0.016$ ), see Figure 1.



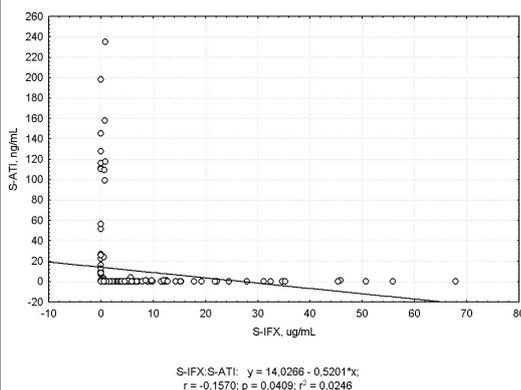
No differences in S-IFX were found in relation to the age, gender or diagnosis.

S-IFX levels in responders were significantly higher compared to secondary non-responders at W2 and W14 ( $p = 0.011$  and  $p = 0.0006$ , respectively) as well as to patients with adverse effects of the treatment ( $p = 0.03$  and  $p = 0.01$ , respectively).

S-ATI were positive in 8/85 (9 %) patients at W2 and 14/85 (17 %) patients at W14. Moreover, absolute values of ATI concentration were higher in W14 samples ( $p = 0.018$ ).

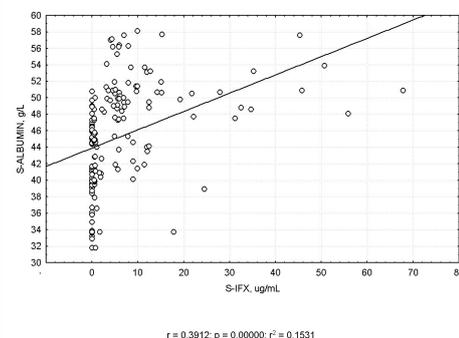
S-ATI were significantly more frequent in samples with non-detectable S-IFX ( $p = 0.041$ ) regardless of the week of the treatment, see Figure 2.

S-ATI achieved the highest values in the group of patients with adverse effects of the treatment ( $p = 0.01$ ).



S-ALB levels were significantly lower at W2 compared to W14 ( $p = 0.0008$ ).

Strong positive correlation between S-ALB and S-IFX was found ( $r = 0.39$ ,  $p < 0.0001$ ), see Figure 3.



Albuminaemia in patients with detectable S-IFX was higher compared to values in sera without detectable S-IFX ( $p < 0.0001$ ).

## Conclusions

S-IFX correlate with the clinical response to treatment with infliximab and S-ALB levels, whereas positive S-ATI are connected with adverse effect of the treatment and occur in sera without detectable S-IFX. This study indicates that patients with starting lower albumin levels might benefit from higher dosages of infliximab or shorter dosing intervals.