**BACKGROUND**

Infliximab (IFX) pre-dose concentrations (C_min) varies greatly between inflammatory bowel disease (IBD) patients. This variability is relevant because there is a relationship between C_min and clinical response. Inter-patient pharmacokinetic (PK) and pharmacodynamic (PD) variability of IFX, clinical outcomes in IBD patients exhibit substantial inter-subject variability. An association between the rs1143634 C allele in IL1B and higher serum IL1B concentrations and a lower response to IFX in Crohn’s disease (CD) patients has been reported. Unraveling the impact of genetic polymorphisms on IFX exposure may help to refine therapy and improve clinical outcomes.

**PURPOSE**

To confirm the effect of the rs1143634 single-nucleotide polymorphism (SNP) of IL1B on IFX exposure and PK in CD and ulcerative colitis (UC) patients.

**RESULTS**

• A total of 67 patients were included. Patient characteristics are shown in Table 1.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Gender (Men/Women), n (%)</th>
<th>Cmin (mg/L), median (Q1-Q3)</th>
<th>ATI positive patients, n (%)</th>
<th>SAC (g/l), median (Q1-Q3)</th>
<th>Cigarette smoking, n (%)</th>
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</thead>
<tbody>
<tr>
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<td>34 (31/33/49)</td>
<td>3.27 (0.75-2.41)</td>
<td>8 (12%)</td>
<td>43 (41-45)</td>
<td>14 (21)</td>
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<td>48 (72)</td>
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<td>44 (66)</td>
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<td>17 (25)</td>
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</table>


• Distribution of allele frequencies and C_min values according to the polymorphism are shown in Figure 1 and Figure 2, respectively.

**CONCLUSIONS**

• IL1B polymorphisms have a major influence on IFX exposure in IBD patients. C allele was correlated with lower C_min and Cmin/D.

**MATERIAL AND METHODS**

• Patients receiving IFX between July 2013 and December 2014 were genotyped for IL1B polymorphism.

• Associations between this SNP and C_min (mg/L), dose-adjusted C_min (Cmin/D, mg/L-1/mg/month-1), area under the concentration-time curve (AUC, mg/h/L) and half-life (t½, days) at steady-state were evaluated.

• Cmin were measured using a validated enzyme-linked immunosorbent assay (ELISA) and polymorphism was determined by PCR.

• This study was approved by Hospital research ethics committee and written informed consent was obtained from each patient.

• Fasamnade AA et al2 population PK model for CD was used in both CD and UC patients.

• PK and statistical analysis was performed using Nonmem®7.2 and SPSS v19, respectively.

**All patients (n=67):**

• Univariate analysis demonstrated that median Cmin, Cmin/D and AUC were statistically lower in carriers C than in TT patients. t½ was significantly lower in CC patients than in CT or TT.

• All patients who developed antibodies toward IFX (ATI) were carriers C (15% of carriers C). 60% of carriers C patients had Cmin < 3 mg/L vs 17% of TT patients.

**ATI negative patients (N=59):**

• 59 patients were ATI negative. The analysis of these patients showed that median Cmin and Cmin/D were significantly lower in C carriers than in TT patients.

**REFERENCES**
