Sa1942

Infliximab Trough Level Measured During Treatment Induction May Be Predictive of the Loss of Response to Infliximab During Treatment Maintenance in Inflammatory Bowel Disease Patients: A Longitudinal Observational Retrospective Study

Claire Liefferinckx, Charlotte Minsart, Anneline Cremer, Jean-François Toubeau, Leila Amininejad, Eric Quertinmont, André Van Gossum, Denis Franchimont, Jacques Devière

Background: Infliximab (IFX), is indicated for the treatment of inflammatory bowel disease (IBD) (ulcerative colitis (UC) or Crohn disease (CD)). Nevertheless, loss of response (LOR) to IFX is reported in up to 20-30% over 12 months of treatment. Importantly, pro-active monitoring of IFX pharmacokinetics may help prevent LOR during treatment maintenance. Our objective is to analyze in a cohort of 263 patients the pharmacokinetics early on in order to predict LOR during maintenance treatment. **Methods**: 263 IBD patients (188 CD and 75 UC) have been treated with IFX on follow-up (median + range), (EC approved). 2331 samples were prospectively collected and measured retrospectively by ELISA in parallel with clinical data. Statistical analysis used Mann- Whitney test after determination of non-normality of compared distributions thanks to χ^2 goodness-of-fit test. **Results**: During the maintenance, the median IFX Trough level (TL) was statistically higher in patients on combo-therapy (IFX combined with immunomodulator, n=107) compared to patients on mono-therapy (n=81) (1.32 µg/ml [0-12.09µg/ml] VS 2.14 µg/ml [0-11.98µg/ml], p<0.000001). Median IFX TL was higher under combo when patients were sequentially treated first with combo- then mono-therapy (4.17 µg/ml [0.12-11.98µg/ml] VS 3.22 µg/ml [0.08-11.98 µg/ml], p < 0.01, n=55). On the contrary, there was no statistical difference between mono- and combo-therapy when patients were sequentially treated first with mono- then combo-therapy (2.02 [0.11-12.09µg/ml] µg/ml VS 2.49µg/ml [0.11-12.09µg/ml], p<0.17, n=49). During maintenance, 19% of the patients (n= 49) experienced LOR, defined as secondary non responders (NRII), requiring treatment optimization by either shortening of the dosing interval and/or by increasing the dose. 57% of these patients (n= 28), defined as secondary non responders end ($NRII_{end}$), did not respond to any optimization strategy and were switched to another treatment, while 43% of patients (n= 21), defined as secondary responders to optimization (RII_{opt}), responded to optimization. Looking at the TLs during induction (week 2 and 6), median IFX TL at induction was not statistically different in NRII (n=49) compared to patients with sustained response (n=170) (6.66 µg/ml [0.23-19.93µg/ml] VS 11.91 µg/ml [0.11-19.93 µg/ml], p <0.08) **(Figure 1).** However, median IFX TL at induction was statistically lower in $NRII_{end}$ (n=23) compared with the patients with sustained response (1.69 [0.30-19.93µg/ml] VS 11.91 µg/ml [0.11- 19.93µg/ml], p <0.05) **(Figure 2). Conclusion:** This study suggests that patients who do not respond to any optimization strategy ($NRII_{end}$) seem to have lower IFX TLs at induction. IFX TLs measured at induction may predict clinical response to IFX during maintenance.

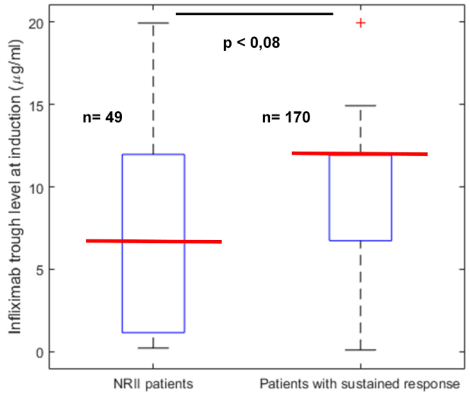

Figure 1. The box plot represents the median IFX TL in induction phase (week 2 and 6) for patients with sustained response (n= 170) and NRII patients (n=49). The interquartile range (25-75%) is represented by rectangle. The whiskers below and above the box represent the limits (2.5% and 97.5%) of the distribution. Median IFX TL is represented by the thick red line. Median IFX TL for NRII patients was 6.66 µg/ml [0.23-19.93µg/ml] and median IFX TL for patients with sustained response was 11.91 µg/ml [0.11-19.93 µg/ml]. There is no statistical difference (p <0.08).

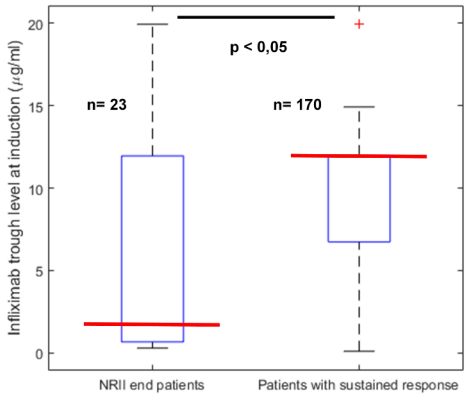

Figure 2. The box plot represents the median IFX TL in induction phase (week 2 and 6) for patients with sustained response (n=170) and $NRII_{end}$ patients (n=23). The interquartile range (25-75%) is represented by rectangle. The whiskers below and above the box represent the limits (2.5% and 97.5%) of the distribution. Median IFX TL is represented by the thick red line. Median IFX TL for NRII patients was 1.69 [0.30-19.93µg/ml] and median IFX TL for patients with sustained response was 11.91 µg/ml [0.11-19.93µg/ml] (p <0.05).

Sa1943

Variability in Vedolizumab Exposure Between Patients With Inflammatory Bowel Disease

Ann Gils, Erwin Dreesen, Miet Peeters, Els Brouwers, Marc Ferrante, Gert Van Assche, Severine Vermeire

Introduction Vedolizumab (VDZ), a humanized monoclonal antibody that specifically targets the $\alpha_4\beta_7$ integrin, has been approved for the treatment of patients with moderate to severe Crohn's disease (CD) and ulcerative colitis (UC), following successful completion of the GEMINI phase 3 programs. Nothing is known about the relation between drug exposure and efficacy in real-life practice. **Aim** Enzyme-linked immunosorbent assays for measuring serum VDZ concentrations and anti-drug antibodies (ADAbs) were developed in house. A total of 37 VDZ naïve patients (24 CD, 13 UC) were sampled at trough during induction treatment (300 mg IV administered at weeks 0, 2 and 6). All patients but one had prior anti-tumor necrosis factor-alpha exposure (table 1). VDZ pharmacokinetics (PK) during induction was described based on trough concentrations and baseline patient factors influencing variability were tested (sex, (lean) body mass, disease type (CD or UC), C-reactive protein (CRP), albumin and lymphocyte count). Biological response, based on CRP, was correlated to the VDZ serum concentrations. **Results** A substantial interindividual variability in VDZ serum concentrations was observed at week 2 (median 27.5 µg/mL, IQR 15.6 µg/mL) and week 6 (median 24.9 µg/mL, IQR 18.8 µg/mL). Two patients with CD had undetectable VDZ trough concentrations at week 6, of which one had detectable ADAbs. No significant difference in week 2 and 6 trough concentrations was seen between CD or UC. Patients with a baseline CRP above 10 mg/L had a significantly lower VDZ trough concentration at week 2 (p=.03). A baseline serum albumin below 40 g/L was associated with significantly lower VDZ trough concentration at week 6 (p=.04). Women had significantly higher VDZ trough concentration at week 2 (p=.0005). A significant negative correlation between (lean) body mass and the VDZ trough concentration at week 2 was found (p=.01 for body mass and p=.001 for lean body mass). Patients who had a decrease in CRP (n=23, excluding ADAb+ patient) between week 0 and week 6 had significantly higher VDZ trough concentrations at week 6 (median 31.7 µg/mL, IQR 20.8 µg/mL), compared to patients who had an increase in CRP (n=13) (median 16.4 µg/mL, IQR 10.8 µg/mL) (p=.046) (figure 1). **Conclusion** This first real-life experience with VDZ shows substantial PK variability between patients. High CRP and low albumin at baseline, both indicators of disease severity, were shown to predict lower VDZ trough concentrations during induction. Higher (lean) body mass is shown to be associated with lower VDZ trough concentrations at week 2. Early biological response, judged by a decrease in CRP by week 6, is associated with significantly higher VDZ exposure at week 6, already suggesting an early exposure-response correlation.
Summary of demographics and baseline characteristics among patients on vedolizumab induction treatment.