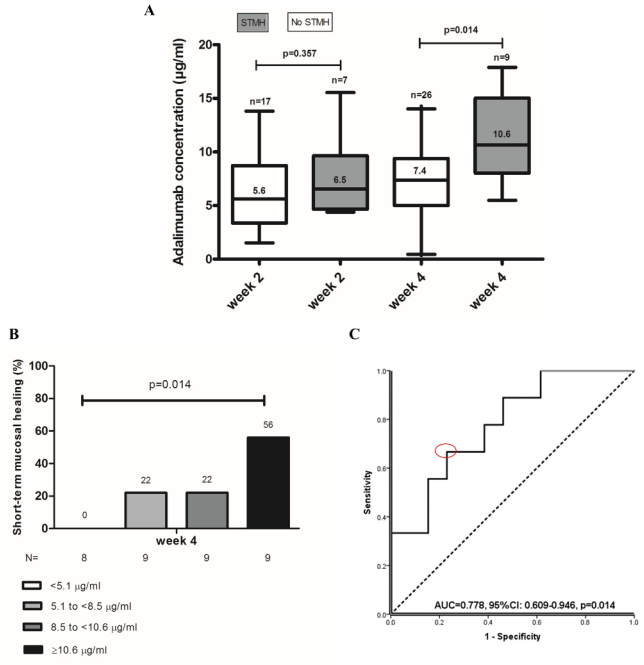

Figure

Sa1957

Switching of Patients With Inflammatory Bowel Disease From Original Infliximab (Remicade®) to Biosimilar Infliximab (Remsima™) Is Effective and Safe

Martin Kolar, Dana Duricova, Martin Bortlik, Veronika Hruba, Nadezda Machkova, Katarina Mitrova, Karin Malickova, Martin Lukas, Milan Lukas

Background: Biosimilar infliximab (IFX) seems to have similar efficacy and safety to original preparation in patients with inflammatory bowel diseases (IBD) who are naïve to anti-TNFa therapy. However, the evidence on switching from original to biosimilar preparation is very sparse. **Aim:** Our aim was to evaluate efficacy and safety of switching from original to biosimilar preparation IFX in patients with Crohn′s disease (CD) and ulcerative colitis (UC). **Methods:** Consecutive patients with CD and UC on maintenance IFX treatment at our center who were switched from original to biosimilar IFX during a period from January to March 2015 were included. Patients were followed prospectively in regular intervals coincident with infusion applications. At each visit disease activity was registered using Harvey-Bradshaw index (HBI) for CD and Simple clinical colitis activity index (SCCAI) for UC; blood sample taken for analysis of blood count, biochemistry and IFX pharmacokinetics (trough levels, TL and anti-drug antibodies, ATI) and stool sample obtained for measurement of fecal calprotectin (FC). Furthermore, adverse events were registered. All patients were evaluated at week 24 (W24) of treatment with biosimilar IFX. **Results**: Seventy-four patients with IBD, 56 with CD and 18 with UC, were switched to biosimilar IFX after mean time of 3±2.2 years on original preparation. Almost half of individuals (34, 46%) were on concomitant azathioprine and one patient had systemic corticosteroids. Majority of patients, 51 (69%) were at the time of switch (week 0, W0) in clinical remission, 16 (22%) had mild to moderate active disease and 4 (5%) individuals had severe disease activity. Comparing W0 and W24, no significant difference in C-reactive protein levels (4.3±8.0 mg/L vs. 3.6±4.5; p=0.78) and FC (135±153 µg/g vs. 226±297; p=0.44) was observed. Likewise, no increase in immunogenicity was found (IFX TL: 3.4±3.8 µg/mL vs. 3.8±3.3, p=0.23; ATI positivity: 9.5% vs. 10%, p=0.79). Furthermore, disease activity was stable until the end of follow-up (remission at W0 vs. W24: 72% vs. 78%). Three patients discontinued IFX treatment up to W22 due to loss of response (n=1), adverse event (n=1) and low grade dysplastic lesion in colon (1 UC patients). None patient experienced infusion reaction and the frequency and type of adverse events were similar to that observed during treatment with original IFX. **Conclusion:** Based on our results switching of IBD patients from original to biosimilar IFX is effective and safe. Importantly, no increase in immunogenicity was observed. **Acknowledgement:** The study was supported by IBD-COMFORT foundation.

Sa1958

No Difference in Immunogenicity of the Original and Biosimilar Infliximab in Patients With Inflammatory Bowel Disease: Short-Term Results

Karin Malickova, Dana Duricova, Martin Kolar, Martin Bortlik, Veronika Hruba, Nadezda Machkova, Katarina Mitrova, Martin Lukas, Milan Lukas

Background: Infliximab (IFX) is a source of potential immunogenicity for patients, with the occurrence of anti-infliximab antibodies (ATI) and different autoantibodies such as antinuclear (ANA), anti-double-stranded DNA (anti-dsDNA), or anti-extractable nuclear antigens (anti-ENA) antibodies. Recently introduced biosimilar IFX seems to be identical to the original drug from the clinical and pharmacological points of view. However, even minor modification of molecular structure could theoretically alter the immunogenicity of the drug. **Aim:** To compare the incidence of immunogenicity to IFX in patients treated by biosimilar and original preparation. **Methods:** Sera from 60 previously IFX-naïve patients treated by the biosimilar IFX (Remsima™) and 71 patients treated by the original preparation (Remicade®) were analyzed at treatment weeks 2 and 14 (W2 and W14) on ATI, ANA, anti-dsDNA and anti-ENA antibodies. ATI were detected by ELISA (Shikari, Matriks Biotek, Turkey). ANA and anti-dsDNA were detected by indirect immunofluorescence (Immuno-Concepts, USA and Orgentec, Germany, respectively), anti-ENA antibodies were analyzed by ELISA (Immco, USA). A X^2 statistic were used to investigate whether distributions of measured qualitative variables differ between two groups. P-values < 0.05 were considered as significant. **Results**: No significant difference in proportion of patients with positive ATI and ANA were observed at W2 between original and biosimilar IFX. None of patients was positive for anti-dsDNA and anti-ENA at W2. Similarly, at W14 the proportion of patients with positive anti-bodies (ATI, ANA, anti-dsDNA and anti-ENA) was not different comparing therapy with original and biosimilar IFX (Table 1). **Conclusion:** Our short-term results demonstrate that original and biosimilar IFX have comparable immunogenicity in patients with inflammatory bowel disease. **Acknowledgement:** The study was supported by IBD-COMFORT foundation.

Table 1

		ATI	ANA	ANA in high titre (1:640)	anti-dsDNA	anti-ENA
W2	Biosimilar IFX	3 %	18%	2%	0%	0%
	Original IFX	10%	14%	3%	0%	0%
	p-value	NS	NS	NS	NS	NS
W14	Biosimilar IFX	7%	30%	18%	3%	2%
	Original IFX	11%	38%	17%	3%	3%
	p-value	NS	NS	NS	NS	NS

Sa1959

Concentrations of 6-Thioguanine Nucleotide Correlate With Both Infliximab and Adalimumab Levels in Patients With Inflammatory Bowel Disease on Combination Therapy

Orlaith Kelly, Aleksander Trajkovski, Adam Weizman, Geoffrey C. Nguyen, A. Hillary Steinhart, Mark S. Silverberg, Kenneth Croitoru

Background: Combining immunomodulators with anti-TNF (tumour necrosis alpha) therapy in Inflammatory Bowel Disease (IBD) is associated with higher anti-TNF levels and possibly mucosal healing. Optimal thiopurine dosing in this context remains unclear. Recent data suggest correlation between 6-Thioguanine (6TG) and infliximab (IFX) levels.We examined if this correlation extended to Adalimumab (ADA) levels and associations with endoscopic remission. **Methods:** A cross-sectional study of IBD patients receiving combination therapy (IFX or ADA + thiopurine) was performed. Patients with simultaneous anti-TNF level/antibody (ADA/IFX; Prometheus assay) and thiopurine metabolite testing (6TG+MMP) were included. Endoscopic remission was defined as Mayo<1 (Ulcerative colitis; UC) or SESCD<3 (Crohn's disease; CD). Primary outcomes were anti-TNF levels and antibody to anti-TNF analyzed as continuous and dichotomized variables with calculated IFX/ADA values best associated with mucosal healing. 6TG levels were examined as continuous and in quartile distribution (1:0-124; 2:125-250; 3:251-400; 4 :>400 pmol/8x10^8 RBC). **Results:** 64 patients on combination were included (34 ADA, 30 IFX). Gender, age, phenotype and treatment duration were not different. All patients were on thiopurines for min. 6 months at testing. Mean 6TG (326, p=0.84) and MMP levels (1572, p=0.07) were similar. Mean IFX and ADA levels were higher in combination compared to a monotherapy cohort (n=122, 12.3 v 10.2 µg/mL IFX, p=0.04, 11.4 v 9.8µg/mL ADA, p=0.04).Antibody presence was lower in combination (10 v16.5%, p=0.04). In those with measurable antibodies, there was also a trend for lower antibodies (2.6 v7.9 U/mL IFX, 3.5 v6U/mL ADA; p=0.26, 0.35 respectively). In combination group, higher anti-TNF levels were associated with endoscopic remission, inversely correlating with Mayo (r=-0.69, p=0.008, AUC 0.6 [0.46-0.83]) and SESCD (r=-0.4, p= 0.039, AUC 0.64 [0.48-0.83]). 6TG levels were associated with higher anti-TNF levels. Based on ROC, using IFX >7.6 mcg/ mL (sens.82% spec.62%), 6TG >125 was associated with adequate (>7.6) IFX levels (p=0.001, r=0.49, Fishers exact p=0.018).Using ADA >6.6 mcg/ mL (sens.83%, spec.54%),6TG >125 correlated with adequate (>6.6) ADA levels (r=0.58, p=0.001, Fishers exact p=0.009). 6TG values in quartiles(Q)2 and 3 (125-400 pmol/8x10^8 RBC) were associated with therapeutic anti-TNF levels (p=0.001) and endoscopic healing (p=0.001). 6TG levels in Q2 and Q3 had fewer antibodies but not significantly.**Conclusions:** Although the accepted range for 6TG for thiopurine monotherapy is 235- 400 pmol/8 x 10^8 RBCs, it has been shown that levels as low as 125pmol/8 x 10^8 correlate with therapeutic IFX levels. Here we extend that concept and show 6TG >125pmol/8 x 10^8 is associated with therapeutic levels of both IFX and ADA and, importantly, with endoscopic remission

Clinical Demographics

Demographic	Total cohort n=64	IFX n=30	ADA n=34	p value
Gender (male)n, %	32; 50	17; 56	15; 45	0.45
Disease type (CD)n %	51; 79	21; 70	30; 88	0.12
Endoscopically active (n, %)	45; 70	16; 53	29; 85	0.005
Clinically active (n, %)	39; 61	15; 50	24; 71	0.08
Age at diagnosis (y, mean , SEM)	21.2±1.2	23±1.5	18±1.6	0.01
Age at anti-TNF initiation (y, mean , SEM)	31.6±1.5	28±2.1	34±2.9	0.08
Age at testing(y, mean , SEM)	34±2.4	30±2.5	36±2.4	0.08
IS at induction of anti TNF (%)	59	46	69	0.07