

of follow-up, during which 42 incident cases of psoriasis were recorded, all of them confirmed by punch biopsies, with an incidence rate of 5 per 100 person-years. Comparing IBD patients with and without skin lesions, we found higher rate of smokers in the subgroup of patients who developed psoriasis (18% vs 36%, $p = 0.01$). Cox-regression survival analysis confirmed smoking as independent predictor of psoriasis (HR 2.37, 95% CI 1.36, 4.48, $p = 0.008$). Concomitant immunosuppressive therapy was inversely related to psoriasis (HR 0.33, 95% CI 0.12, 0.92, $p = 0.03$).

Conclusions: New onset of psoriasis is a relevant side effect of anti-TNF α therapy with an incidence rate of 5 per 100 person-years. Smoking is confirmed as the main risk factor for developing lesions. The combination therapy with anti-TNF α plus immunosuppressants was associated with a reduced risk for psoriasis.

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Tacrolimus suppositories in therapy-resistant ulcerative proctitis - a single center experience

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Background: Ulcerative proctitis may be often managed with topical salicylates or budesonide alone, but in some patients, symptoms can be persistent, severe and have a profound impact on quality of life. Here we present an analysis from our outpatient clinic with add-on therapy of tacrolimus suppositories in patients who remained symptomatic despite conventional systemic and topical therapy.

Methods: We followed up 25 patients with ulcerative proctitis (E1, Montreal classification). Patients already received oral therapy consisting of an immunomodulator, prednisolone, salicylates and topical treatment with steroids or salicylates. CAI according to Rachmilewitz was assessed at start of tacrolimus treatment and at every follow-up visit. The content of one 2 mg capsule of tacrolimus was moulded into suppositories by our pharmaceutical department. Patients took 1 suppository BID. Tacrolimus serum levels, CRP, complete blood count and ESR along with creatinine were assessed via routine laboratory. Data was analyzed with Graph Pad Prisms.

Results: Median time from baseline to a consultation with assessment of CAI and tacrolimus serum level was 75 days. Three patients discontinued treatment after they experienced worsening of symptoms. Including these treatment failures, patients showed a significant decrease in CAI from 7,8 to 5,7 points ($p=0,0279$).

Mean tacrolimus trough level ($n = 17$) was 5,25 ng/mL (SD +/-2,601). The mean time from application of the last suppository was 17,6 hours (SD +/-6,862). The highest individual level was 10,2 ng/mL. We furthermore found a significant, moderate correlation between the change in CAI from baseline to follow-up and the height of tacrolimus trough level (Spearman $r -0,555$ (95% CI -0,8291 to -0,0657; $p = 0,025$). In terms of side effects, we registered 1 case of hypertension, 2 cases of tingling sensation in hands and feet and tremor, 1 case of headache, muscle cramps at night and unspecific fatigue.

Conclusions: After addition of a topical formulation of tacrolimus (suppositories) in ulcerative proctitis refractory to standard treatment, we observed a significant decrease in CAI scores over a median treatment duration of 75 days. Mean tacrolimus serum levels were

5,253 ng/mL, and clinical benefit positively correlated with the height of serum levels. As envisioned by the use of topical treatment, side effects were rare and mild. On the other hand, tacrolimus serum levels were high enough to suggest that clinical benefit might be due to systemic tacrolimus effects. In this retrospective, observational study from our outpatient clinic, tacrolimus suppositories were used with success. Nevertheless, a further prospective study is needed to confirm these findings.

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A prospective evaluation of adalimumab drug levels and anti-drug antibodies using two commercial ELISA and the influence of 6-thioguanine nucleotides amongst patients with Crohn's disease

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Background: Some [1],[2] but not all [3] studies have demonstrated a relationship between therapeutic drug monitoring (TDM) of adalimumab (ADA) and outcomes in Crohn's disease (CD). We evaluated the utility of TDM of ADA in patients with CD using two commercially available ELISA

Methods: ADA drug levels (DL) and anti-drug antibodies (ADAb) were measured in CD patients ($n=80$) from 2 tertiary referral centres, between November 13 and February 14 using the Lisa-Tracker Duo ((LT) Theradiag, France) and Immundiagnostik ELISA ((IM) Germany). Faecal calprotectin (FC), C-reactive protein(CRP;<5ng/mL remission) and clinical activity (Harvey Bradshaw Index,(HBI)<5 remission) were also recorded. LT kits were provided by Theradiag at no cost.

Results: Neither assay showed a significant difference in ADA DL between remission and active disease (Table 1).

No significant differences in DL were observed in TDM performed at trough (day 13 or 14, $n=13$) or at any other time in the treatment cycle, nor amongst those receiving ADA every other week compared to weekly. Thiopurine metabolites (TGN) were performed in 51/52 patients taking thiopurines, (median 302, IQR 242-411 pmol/ 8×10^8). There was no significant difference between DL and TGN according to TGN quartiles. ADAb were detected in 1(1.3%) patient using LT and 4(5%) using IM. Concomitant immunomodulation or therapeutic TGN(>235) did not significantly influence median DL or the detection of ADAb with either assay. IM ADA showed proportional positive bias (79.6%) against LT (Passing Bablok regression $IM= 1.74 LT - 0.06$)

Conclusions: No optimal cut-off could be identified that predicted clinical or biochemical remission or FC. Concomitant immunomodulation and TGN concentration was not associated with higher ADA DL. ADAb development was very rare whether measuring free (LT) or total (IM) ADAb. Further studies are needed to establish the cause of DL variation and understand differences in ADA pharmacokinetics in patients with CD.

"Table 1"

Outcome	Theradiag (LT)					Immundiagnostik (IM)				
	Remission		Active Disease			Remission		Active Disease		
	n (%)	DL*	n (%)	DL*	p value	n (%)	DL*	n (%)	DL*	p value
FCP<250 µg/g	57 (71)	6.2	23 (29)	5.7	0.3	57 (71)	11.1	23 (29)	10.1	0.2
FCP<59 µg/g	32 (40)	6.1	48(60)	5.9	0.4	32 (40)	11.3	48 (60)	10.4	0.6
CRP(<5) g/L	66 (85)	6.1	12(15)	5.4	0.6	66 (85)	11	12 (15)	9.8	0.6
HBI	66 (83)	6.1	14 (17)	5.5	0.7	66 (83)	11	14 (17)	10.4	0.6

*median DL (µg/mL).

References:

- [1] Mazor Y, (2014), Adalimumab drug and antibody levels as predictors of clinical and laboratory response in patients with Crohn's disease, *Alimentary Pharmacology and Therapeutics*, 620-628
- [2] Roblin X, (2014), Association Between Pharmacokinetics of Adalimumab and Mucosal Healing in Patients With Inflammatory Bowel Diseases, *Clinical Gastroenterology and Hepatology*, 80-84
- [3] Chiu Y-L, (2013), Serum Adalimumab Concentration and Clinical Remission in Patients with Crohns Disease, *Inflammatory Bowel Diseases*, 1112-1122

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Change in clinical features of Korean Crohn's Disease patients following the introduction of an anti-TNF-alpha agent: Results from the CONNECT study

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Background: Background: Anti-tumor necrosis factor-alpha (anti-TNF-alpha) agents have been known to alter the natural course of Crohn's disease (CD). Therefore, we aimed to compare the changes in clinical features and disease course according to the time of introduction of an anti-TNF-alpha agent in Korea.

Methods: Methods: We performed a retrospective analysis of 1,382 Korean CD patients diagnosed between 1982 and 2008 who were enrolled in the retrospective cohort of the Crohn's disease clinical Network and Cohort (CONNECT) study. The anti-TNF-alpha agent was applied to national medical insurance in 2005, and has been more widely used in Korea since 2007. Accordingly, the patients were divided into three groups [Group A (1981-2004): 656 patients; Group B (2005-2006): 282 patients; and Group C (2007-2008): 362 patients].

Results: The average age ($p = 0.251$), disease location ($p = 0.941$), and disease behavior ($p = 0.813$) at the time of diagnosis with CD were not different among the three groups. The anti-TNF-alpha agent was administered to a total of 31.0% of patients ($n = 403$), which was not different among groups ($p = 0.124$).

However, the 3- and 5-year cumulative probabilities for administering an anti-TNF-alpha agent were significantly higher in group C ($p < 0.001$). The 3- and 5-year cumulative probabilities of the occurrence of perianal fistula and CD-related surgery were higher in group A than in group C (perianal fistula, $p = 0.032$; surgery, $p = 0.003$).

Conclusions: Conclusions: After the introduction of the anti-TNF-alpha agent to the treatment of Korean CD patients, the natural history of CD changed. We found that early administration of an anti-TNF-alpha agent may help delay the occurrence of perianal fistula and the need for surgery in Korean CD patients.

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Inflammatory Bowel Disease Patient's Participation in Therapeutic Decision Making

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Background: Non-adherence to medical treatment in patients with inflammatory bowel disease (IBD) is a matter of a grave concern. Active participation in therapeutic decision making, as one of the aspects of patient empowerment, has potential to increase adherence to therapy. However, data from large studies on patients' participation in therapeutic decision making in IBD is scarce. Therefore, we aimed to evaluate the patients' role in therapeutic decision making.

Methods: A paper-based 15-item questionnaire was developed by IBD experts and sent to 2,100 members of the Swiss Association of IBD patients in September, 2014. In addition to patient baseline characteristics, the patients were asked about their experience in regards to developing a therapeutic concept together with their treating gastroenterologist.

Results: A total of 824/2,100 (39.2%) adult IBD patients sent back the completed questionnaires. Of these patients, 66% were female, 57% had CD, 41% had UC, and 2% had unclassified IBD. The age distribution was as follows: 31% were aged up to 40 years, 47% were between 41-60 years, and 22% were > 60 years old. When being asked "How actively were you involved in therapy decisions?" patients chose the following options: 50% told that their gastroenterologist proposed one particular therapy regimen which they followed, 23% told that their gastroenterologists provided them with several therapeutic options of which they chose one, 8% of patients told that they read about various therapeutic options on the internet before discussing their therapy of choice with the gastroenterologist, 7% told that due to their activity in the IBD patients organization they already made their mind about a particular therapy option which they proceeded to discuss with their gastroenterologist, 7% of patients told that they decided for another therapy than the one recommended by their gastroenterologist, and 5% of patients noted that their gastroenterologist provided them with several therapy options, but they thought it is upon the gastroenterologist to select the appropriate treatment. Older patients (55 years of age and older) were more likely to choose the option that it is upon the gastroenterologist to select the appropriate treatment when compared to younger patients (< 55 years) (12.7% vs.