($p < 0.05$) and median DCA 2 [1–5] pmol/mg vs. 2605 [29–4288] pmol/mg ($p < 0.05$). NSR patients also exhibited higher levels of primary BA (cholic acid (CA) and chenodeoxycholic acid (CDCA)) at baseline and Week 12, although this was not significant. The ratio of primary to secondary BAs was profoundly increased in NSR patients compared with SR patients: median 318.4 [0.926–642.1] ($p < 0.05$) vs. median 0.005 [0.002–0.059]. Levels of primary and secondary BA did not change significantly over the course of EEN in either group, although secondary BA concentrations were slightly increased in NSR patients by Week 12 relative to baseline.

Conclusions: We demonstrate that primary and secondary BA compositions in stool differed between patients who sustained remission following EEN vs. those who relapsed. BA profiling may be a useful microbiome metabolic marker to identify patients who will sustain remission longer following EEN therapy.

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Golimumab dried blood spot analysis (GOUDA): A prospective trial to validate golimumab concentration analysis using the dried blood spot methodology

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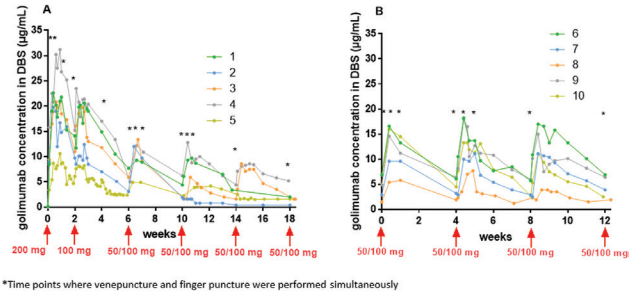
Background: Therapeutic drug monitoring of golimumab (GLM) is performed by measuring trough concentrations, obtained by venous sampling. Sampling via dried blood spots (DBS) allows multiple determinations within a dosing interval and thereby gives a more complete insight in the total drug exposure (here expressed as area under the curve or AUC). We assessed the robustness and user-friendliness of the DBS method and the relation between GLM trough concentration (TC) and exposure during induction and maintenance regimens.

Methods: Ten patients with ulcerative colitis (UC) were recruited prospectively (NCT02910375). Finger and venepunctures were performed according to the sampling schedules depicted in Figure 1A and B in five patients initiating GLM and in five patients on ≥2 years GLM maintenance therapy. At the end of the study, user-friendliness was evaluated using a questionnaire. GLM and anti-GLM antibody concentrations were measured using in-house developed ELISAs.[1] Non-compartmental pharmacokinetic evaluation was performed using the PKNCA R package. Mucosal healing (Mayo endoscopic sub-score ≤1) was evaluated at Week 14. Data are expressed as mean ± SD.

Results: A total of 79 matched pairs of serum and DBS sample GLM concentrations showed a very good correlation (Spearman $r = 0.990$, $p < 0.0001$). Nine out of 10 patients reported DBS sampling as user-friendly. For patients initiating therapy, TC were not linearly correlated with AUC ($R^2 = 0.29$). In these patients, a significant decrease in TC was observed from Week 2 (11 ± 4.1 µg/ml) to Week 10 (3.3 ± 1.9 µg/ml) ($p = 0.005$) but not in AUC within the respective dosing intervals ($AUC_{0–2}$ = 212 ± 82.4 µg day/ml vs. $AUC_{6–10}$ = 175 ± 50.6 µg day/ml) ($p = 0.085$). This decrease in TC was more pronounced in patients without mucosal healing (patients 1–3) than in patients with mucosal healing (patients 4 and 5) ($p = 0.028$). During maintenance phases, a trend for lower TC and AUC were observed in patients starting therapy (Weeks 6–18) than in patients who were treated for ≥2 years ($p = 0.064$ and 0.053). Using a drug-tolerant assay, anti-GLM antibodies were detectable in two starters and in one patient on maintenance therapy.



*Time points where venepuncture and finger puncture were performed simultaneously

Figure 1. (A) GLM concentration vs. time profiles of patients who started GLM therapy. Patients 4 and 5 achieved mucosal healing (B) GLM concentration vs. time profiles of patients on ≥2 years GLM maintenance therapy. All patients had achieved mucosal healing.

Conclusions: The GOUDA study showed that DBS sampling is a robust and patient-friendly alternative to venous blood collection. DBS sampling provides also better insights into GLM exposure, as exposure was not captured well by the TC during induction. The GOUDA data are currently pooled with two other datasets to determine the GLM exposure-response relationships.

Reference

1. Detrez et al. Variability in golimumab exposure: a 'real-life' observational study in active ulcerative colitis. *J Crohns Colitis*, 2016;10(5): 575–81.

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Does medical acceleration improve long-term outcomes in ulcerative colitis patients who are in clinical remission but have endoscopic mucosal inflammation?

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Background: Discrepancies between clinical symptoms and mucosal inflammation have been reported in up to 50% of patients with ulcerative colitis (UC). However, there are no guidelines and only limited information for appropriate treatment manipulation in these patients. We aimed to evaluate long-term outcomes according to treatment strategies and determine predictive factors for disease relapse in UC patients who are in clinical remission (CR) but still have endoscopic inflammation.

Methods: A total of 204 patients who were confirmed as achieving CR but still had active mucosal lesions were included. CR was defined as 'partial Mayo score ≤ 1' with no changes in medications or use of any corticosteroids during the past 3 months. An active mucosal lesion was defined as "endoscopic Mayo subscore > 0."

Results: The mean patient age was 43.5 years, and 53.9% of the included patients were male. The mean disease duration was 89.9 months. During a mean follow-up of 34 months, 90 patients (44%) experienced disease relapse. The cumulative relapse-free rate did not differ by treatment strategy (maintenance of current therapy vs. dose elevation or step-up therapy). Multivariate analysis revealed that left-side colitis or pancolitis at diagnosis (OR, 2.10; 95% CI 1.04–4.27; $p = 0.040$) and number of extraintestinal manifestations ≥ 2 (OR, 5.62; 95% CI 1.10–28.68; $p = 0.038$) were independent predictive factors for disease relapse.

Conclusions: The current medical acceleration treatment strategy did not have a significant influence on the long-term outcomes of UC patients in CR but with active mucosal inflammation. Disease extent

at diagnosis and extraintestinal manifestations were independently predictive of disease relapse.

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Faecal calprotectin is correlated to endoscopic disease activity at Week 16 in IBD patients on vedolizumab therapy

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Background: A reliable correlation between faecal calprotectin (FCP) and endoscopic response after initiation of VDZ would help to objectify response to VDZ. We aimed to assess the correlation between FCP and endoscopic findings 16 weeks after initiation of VDZ.
Methods: Prospective inclusion of adult patients with CD, UC and IBD unclassified (IBDU) who started VDZ between October 2014 and August 2017 with FCP data at baseline and 16 weeks. Endoscopic disease activity was assessed at baseline and at Week 16. Endoscopic remission was defined as SES-CD <4 or Rutgeerts score ≤1 for CD patients and endoscopic MAYO score ≤1 for IBDU and UC patients. Endoscopic response was defined as SES-CD reduction ≥50%, Rutgeerts reduction of ≥1 and MAYO score reduction of ≥1. Endoscopic scores were categorised in no mild–moderate or severe inflammation. Correlation analysis was done with Pearson statistics.
Results: The study population comprised 26 CD, 14 UC and 5 IBDU patients, 40% males with a median age of 41 years (IQR 36–54). In total 42 of 45 (93%) patients received previous anti-TNFα therapy, of whom 71% were anti-TNFα refractory. The start of VDZ was combined with corticosteroid induction therapy in 27 of 45 (60%) patients. The median FCP levels decreased from 956 µg/g (IQR 347–1800) at baseline to 291 µg/g (IQR 108–1196) at Week 16 ($p = 0.012$). A total of 22 of 45 (49%) patients were in endoscopic remission and 27 of 45 (60%) reached endoscopic response at Week 16, with no significant differences between CD and UC. FCP at Week 16 is positively correlated to Week 16 endoscopic findings ($r = 0.46$, $p = 0.001$). The correlation was observed for both subpopulations of CD $r = 0.45$ ($p = 0.02$) and UC patients $r = 0.52$ ($p = 0.02$). Repeated measures test showed a decrease in FCP is positively correlated to a decrease in severity of inflammation $r = 0.76$ ($p = 0.011$). In separate analysis for CD and UC, this correlation was only significant in UC $r = 0.58$ ($p = 0.04$). Using ROC statistics, a cut-off value of 50% decrease in FCP indicated endoscopic remission with a sensitivity of 82% and a specificity of 70% (AUC = 0.75) PPV = 69% and NPV = 79%. Vice versa, an absolute cut-off value of FCP ≥ 270 indicates endoscopic no remission with PPV of 68% and NPV of 70%.
Conclusions: FCP levels correlate significantly with mucosal disease activity in a tertiary IBD population treated with VDZ for 16 weeks. A 50% decrease in FCP as compared with baseline or FCP ≥ 270 after 16 weeks of VDZ treatment are reasonably reliable markers of endoscopic remission.

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Remission induction in corticosteroid naive children and adolescents with active ulcerative colitis by adsorptive leucocytapheresis after failure of first-line medications: Results from routine clinical practice

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Background: In patients with active ulcerative colitis (UC), myeloid lineage leucocytes are elevated with activation behaviour including the CD14+CD16+ monocytes, which are a major source of tumour necrosis factor-α (J Immunol 2002;168: 3536–42). Therefore, selective depletion of myeloid leucocytes by adsorptive granulocyte/monocyte apheresis (GMA) with an Adacolumn is expected to promote remission, or enhance drug efficacy. Potentially, GMA should be a favourable option when drug therapy has limitations.
Methods: In clinical practice setting, 30 consecutive children/adolescents with active UC, age 11–19 years, body weight 33–55.5 kg were given mesalazine ($n = 23$) or sulphasalazine ($n = 7$) as first-line medication. Patients who did not achieve remission were to receive GMA with the Adacolumn. Twenty patients relapsed while receiving first-line medication or did not respond and received GMA, at two sessions in the first week, then weekly, up to 11 sessions. Patients who achieved ≥5 points decrease in the clinical activity index (CAI) continued with GMA, while non-responders received GMA plus a low dose prednisolone (0.5–1.0 mg/kg). At entry and Week 12, patients were clinically and endoscopically evaluated with each patient serving as her or his own control.
Results: At entry, all patients were corticosteroid naïve and none had deep colonic UC lesions or extensive loss of the mucosal tissue at the affected sites (GMA non-responder features). Ten patients achieved stable remission with the salicylates and did not receive GMA. Six patients did not respond well to the first five GMA sessions and received prednisolone together with GMA, 12 patients achieved stable remission with GMA and two withdrew to receive high dose prednisolone. At entry, the average CAI was 14.2 ± 0.4, range 11–17, and the average endoscopic index was 9.2 ± 0.4, range 7–11. The corresponding values at Week 12 were 2.1 ± 0.2 range 1–4 ($p < 0.001$) and 2.4 ± 0.2, range 1–4 ($p < 0.001$), respectively. Prednisolone was tapered to 0 mg within 3 months in those who received to induce remission. Therefore, at Week 12, all 30 patients were in remission, majority with mucosal healing.
Conclusions: GMA in young corticosteroid naïve patients with active UC refractory to the first-line salicylates-induced clinical remission and mucosal healing, while in non-responders to GMA monotherapy, addition of a low dose prednisolone enhanced the efficacy of GMA and tapering of the prednisolone dose was not associated with relapse. Therefore, the majority of young steroid naïve UC patients who fail to respond to the first-line salicylates should respond well to GMA and avoid pharmacologicals. Additionally, GMA has a good safety profile, which is a very favourable feature in growing patients.

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Effectiveness of therapeutic drug monitoring of infliximab and adalimumab in inflammatory bowel disease patients. Systematic review and meta-analysis

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Background: About one-third of IBD patients do not attain a clinically relevant response to the induction series with anti-TNF and about half of those with initial response lose effect during the maintenance phase. Guidelines suggest handling anti-TNF treatment failure by an "empiric" strategy, i.e. intensifying treatment regimen, switching within drug class or to another agent with different mechanism of action. Therapeutic drug monitoring by measurements of circulating anti-TNF drug levels and antidrug antibodies enables