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Mucosal Healing and Long-term Outcomes of Patients With Inflammatory Bowel Diseases Receiving Clinic-based vs Trough Concentration-based Dosing of Infliximab

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Disclosures

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Author contributors

LP performed research and statistical analysis, interpreted data and drafted the manuscript.

MF, GVA, PR and MN interpreted data and critically revised the manuscript. JS performed

statistical analysis and interpreted data. NVC performed research, interpreted data and

critically revised the manuscript. AG interpreted data and critically revised the manuscript.

SV designed the study, interpreted data and critically revised the manuscript.

All authors approved the final published version of the manuscript, and are accountable for all aspects of this work.

Abbreviations

ATI: antibody to infliximab

CD: Crohn's disease

IBD: inflammatory bowel disease

IQR: interquartile range

TAXIT: Trough Concentration Adapted Infliximab Treatment

TDM: therapeutic drug monitoring

TNF: tumour necrosis factor

UC: ulcerative colitis

ABSTRACT

Background & Aims: The trough concentration adapted infliximab treatment (TAXIT) trial demonstrated that maintaining infliximab trough concentrations at 3–7 µg/mL is most effective at inducing remission in patients with inflammatory bowel diseases (IBD), with fewer flares than clinic-based dosing. We performed a follow-up analysis of study participants to explore the correlation between trough dosing strategy and mucosal healing, continued infliximab use, and rates of hospitalization, surgery, and steroid use.

Methods: This was a retrospective single-center study of 226 patients with IBD who completed the maintenance phase of TAXIT, performed at the University Hospitals of Leuven in Belgium. Baseline patient characteristics, laboratory test results, and endoscopic data were obtained at the end of that study between June 2012 and December 2013 (n=125). Long-term outcome data (IBD-related hospitalization, abdominal surgery, and systemic steroid use) were collected from the time of the last TAXIT study visit (August 2012–April 2013) until April 1st, 2016. We also collected data on continued use of infliximab and trough concentrations.

Results: At baseline, 91% of patients in the clinic-based dosing group and 90% of patients in the trough concentration-based dosing group had mucosal healing. After a median follow-up time of 41 months (interquartile range, 39–42 months), infliximab treatment was continued by 81/108 patients (75%) from the clinic-based dosing group and 86/107 (80%) from the trough concentration-based dosing group. However, within 1 year, infliximab was discontinued by 10/27 patients (37%) patients from the clinic-based dosing group and 2/21 patients (10%) from the trough concentration-based dosing group ($P=.04$). The rates of hospitalization, surgery and steroid use were below 15% in both groups.

Conclusion: At the end of a trial of clinic-based dosing vs trough concentration-based dosing of infliximab in patients with IBD, most patients had mucosal healing. Most patients (75% or more) in both groups continued taking infliximab for more than 3 years after the trial, but a significantly higher proportion of patients in the clinic-based dosing group discontinued infliximab in the first year after the end of the trial. Both groups had low rates of hospitalization, surgery and steroid use.

KEY WORDS: endoscopic, TNF antagonist, therapeutic drug monitoring, optimization

INTRODUCTION

A significant proportion of inflammatory bowel disease (IBD) patients treated with anti-tumour necrosis factor (TNF) therapy lose response over time.[1] One of the reasons for loss of response is immunogenicity or formation of antibodies against anti-TNF therapy.[2,3] Measuring drug levels and anti-drug antibodies and adjustment of the dose when needed is called therapeutic drug monitoring (TDM). TDM offers the opportunity to determine the most appropriate therapeutic strategy in anti-TNF therapy treated patients losing response.[4] There is growing evidence that TDM improves patient outcomes and is cost-effective, although more data are needed.[5,6]

In the Trough Concentration Adapted Infliximab Treatment (TAXIT) trial, 263 IBD patients with a stable response to infliximab maintenance therapy were included. [7] TDM was applied proactively and the infliximab dosing regimen was first escalated or reduced to reach target infliximab trough concentrations of 3-7 µg/mL in every patient (optimization phase). After that, patients were randomly assigned (1:1) to the clinic-based dosing arm, with infliximab dosing based on clinical features, or to the concentration-based dosing arm, with infliximab dosing based on trough concentrations (maintenance phase). The optimization phase of TAXIT showed that targeting infliximab trough concentrations between 3-7 µg/mL resulted in a more efficient use of the drug. In maintenance phase, continued concentration-based dosing was not superior to clinic-based dosing for achieving the co-primary endpoint of clinical and biochemical remission after 1 year, however fewer flares were seen in the concentration-based dosing arm.[7]

In this follow-up analysis of all patients that completed the maintenance phase of TAXIT, we aimed to explore the correlation between drug level-based dosing and endoscopic healing at the end of TAXIT and between the durability of response and important outcome parameters (IBD-related hospitalization, abdominal surgery, steroid use) during long-term follow-up after

TAXIT.

METHODS

Study design and population

This was a retrospective single-centre study of all IBD patients that completed TAXIT maintenance phase, at the University Hospitals Leuven, Belgium. The Supervisory Committee of Medical Ethics at the University Hospitals Leuven approved the study.

Data collection

Baseline patient characteristics

Baseline patient characteristics were derived from the original database at the end of TAXIT maintenance phase. Infliximab trough concentrations and antibody to infliximab (ATI) concentrations during TAXIT were measured using a first generation, in-house developed ELISA.[8] The lower limit of quantification for infliximab and ATI was 0.3 µg/mL and 1.0 µg/mL equivalents, respectively. ATI concentration was determined with a drug-sensitive assay.

Endoscopic findings

All available data of endoscopies performed at the end of TAXIT were analysed. We considered endoscopies eligible for inclusion if performed during the last 4 months of TAXIT maintenance phase or in the first 8 months after the end of TAXIT maintenance phase. All endoscopies were performed between June 2012 and December 2013 by 1 of 3 experienced IBD staff with video and photo documentation. Endoscopies in Crohn's disease (CD) were rated as 'absence of ulcerations' or 'clear improvement of ulcerations compared to baseline endoscopy' or 'no clear improvement or worsening of ulcerations compared to baseline

endoscopy'. Endoscopies in ulcerative colitis (UC) were rated by using the Mayo endoscopic subscore, ranging from 0 to 3. Eventually, 'mucosal healing' was defined as the 'absence of ulcerations' or as 'clear improvement but persistent ulcerations when compared to baseline endoscopy' (for CD) and as a 'Mayo endoscopic subscore ≤ 1 ' (for UC). 'Complete mucosal healing' was defined as the 'absence of ulcerations' (for CD) and as a 'Mayo endoscopic subscore ≤ 1 ' (for UC).

Long-term outcome data

Long-term outcome data were collected from the electronic charts of the patients between the time of the last TAXIT study visit (first to last patient out August 2012 to April 2013) until April 1st, 2016. Infliximab trough concentrations and ATI concentrations during long-term follow-up after TAXIT were measured using a second generation, in-house developed ELISA assay. [9,10] The lower limit of quantification with this second generation assay also was 0.3 $\mu\text{g/mL}$ for infliximab, but was 5 ng/mL equivalents MA-infliximab10F9 for ATI. ATI concentration was determined with a drug-sensitive assay.

Statistical analysis

Statistical programs GraphPad (QuickCalcs) and R version 3.3.0 for Windows (2016 The R Foundation for Statistical Computing) were used for statistical analysis. Data were expressed as medians and interquartile range (IQR) unless stated otherwise. For the univariate analysis of discrete variables, Fisher's exact test or X^2 was used were appropriate. Shapiro-Wilk normality test was used to assess the normality of continuous variables. For the univariate analysis of unpaired continuous variables, either an unpaired t test or independent 2-group Mann-Whitney U test was used. A paired t test or Wilcoxon signed rank test was used for paired continuous variables as appropriate. For time to event analysis, a Kaplan-Meier graph

was constructed. $P < .05$ was considered statistically significant.

RESULTS

Baseline patient characteristics

In total 226 IBD patients completed TAXIT maintenance phase. Baseline characteristics are shown in table 1.

Endoscopic findings

Of all patients completing TAXIT maintenance phase, 125 (55%) underwent endoscopy ($n=55$ in clinic-based dosing arm and $n=70$ in concentration-based dosing arm). Indications for endoscopy were documentation of luminal disease activity in patients with clinical or biochemical suspicion of relapse or in patients who never had a control endoscopy after baseline endoscopy at diagnosis, and surveillance. Endoscopy was not mandatory at the end of TAXIT and was missing in 101 patients. Of those, 48 patients already had mucosal healing at the start of TAXIT and therefore endoscopy was not repeated. In 19 patients, endoscopy was not the preferred tool of follow-up, because of predominant perianal involvement (14 patients) or upper gastro-intestinal tract involvement (5 patients). For 34 patients, we could not find a definite reason for not performing endoscopy.

Characteristics of patients with eligible endoscopy are shown in table 2.

Endoscopic findings at the end of TAXIT by treatment arm

Overall, similar rates of mucosal healing were observed in patients after clinic-based compared to concentration-based dosing (91% vs. 90%, $P=1$). The rates of mucosal healing were comparable between both arms in CD (35/38 patients in clinic-based dosing arm vs. 49/52 patients in concentration-based dosing arm, $P=.69$) and in UC separately (15/17

patients in clinic-based dosing arm vs. 14/18 patients in concentration-based dosing arm, $P=.66$) (figure 1). The rates of complete mucosal healing in the overall population were 89% in patients after clinic-based dosing and 74% in patients after concentration-based dosing ($P=.04$).

Correlation between endoscopic findings and the combined endpoint of clinical and biochemical remission at the end of TAXIT

Mucosal healing was seen in 79/84 (94%) patients who reached the combined primary endpoint of clinical and biochemical remission (defined as either a Harvey-Bradshaw Index < 5 in CD or a Partial Mayo Score < 3 with no individual subscore of > 1 in UC, in combination with C-reactive protein ≤ 5.0 mg/L) after maintenance phase of TAXIT and in 34/41 (83%) patients who did not reach the primary endpoint ($P=.06$). Complete mucosal healing was seen in 73/84 (87%) patients who reached the primary endpoint of TAXIT and in 28/41 (68%) patients who did not reach the primary endpoint ($P=.02$).

Correlation between endoscopic findings at the end of TAXIT and the need for rescue therapy during TAXIT

Mucosal healing was seen in 9/12 (75%) patients who needed rescue therapy because of disease flare-up during maintenance phase of TAXIT and in 104/113 (92%) of patients who did not need rescue therapy ($P=.09$). Complete mucosal healing was seen in 7/12 (58%) patients who needed rescue therapy during maintenance phase of TAXIT and in 94/113 (83%) patients who did not need rescue therapy ($P=.05$).

Correlation between endoscopic findings at the end of TAXIT and serum trough concentration during TAXIT

The median serum trough concentration during maintenance phase of TAXIT was 5.06 µg/mL (IQR 4.27-6 µg/mL) in patients with mucosal healing at the end and 4.33 µg/mL (IQR 4.05-5.29 µg/mL) in patients without mucosal healing ($P=.11$). The median serum trough concentration during maintenance phase of TAXIT was 5.03 µg/mL (IQR 4.27-5.94 µg/mL) in patients with complete mucosal healing at the end and 5.20 µg/mL (IQR 4.19-6.64 µg/mL) in patients without complete mucosal healing ($P=.56$).

Long-term outcome data

Median follow-up time after TAXIT maintenance phase was 41 months (IQR 39-42 months). In total, 11 out of 226 patients were lost to follow-up, leaving 215 patients available for analysis (108 patients previously randomized to clinic-based dosing and 107 patients to concentration-based dosing). Regardless of previous randomization arm, all patients were treated according to routine clinical practice in our hospital after completion of TAXIT maintenance phase, with regular (approximately 1x/year proactively and supplementary in case of suspicion of loss of response) drug monitoring and dose adaptations if trough levels were not in the therapeutic interval of 3-7 µg/mL.

Durability of response to infliximab

At the end of follow-up, 81/108 patients (75%) previously randomized to clinic-based dosing vs. 86/107 patients (80%) previously randomized to concentration-based dosing were still on continued infliximab treatment ($P=.41$). In total, 48/215 patients stopped infliximab. Reasons to stop infliximab are shown in table 3.

After discontinuation of infliximab 24 patients received no other treatment, 5 patients

underwent surgery, 12 patients were switched to vedolizumab, 3 patients to adalimumab and 4 patients to experimental therapy.

Time to discontinuation of infliximab

At the end of follow-up, time to stop infliximab did not differ between the two previous treatment arms of TAXIT ($P=.28$) (figure 2). Among the 48 patients who discontinued infliximab, 10/27 (37%) randomized previously to clinic-based dosing did so within 1 year after the study, compared to 2/21 (10%) patients randomized to concentration-based dosing ($P=.04$). Discontinuation of infliximab in the first year because of loss of response or immunogenicity was observed in 5/11 patients (45%) previously randomized to clinic-based dosing, compared to 1/10 patients (10%) previously randomized to concentration-based dosing ($P=.15$). One year after completion of TAXIT maintenance phase, there were 5 patients with detectable ATI and all had been randomized before to the clinic-based dosing arm ($P=.11$).

IBD-related hospitalization, abdominal surgery and steroid use

During long-term follow-up after TAXIT, the rate of IBD-related hospitalization was 14/108 (13%) in patients previously randomized to clinic-based dosing and 16/107 (15%) in patients previously randomized to concentration-based dosing ($P=.70$). The rate of IBD-related abdominal surgery was 6/108 (6%) in patients previously randomized to clinic-based dosing and 8/107 (7%) in patients previously randomized to concentration-based dosing ($P=.60$). The rate of steroid use was 14/108 (13%) in patients previously randomized to clinic-based dosing and 9/107 (8%) in patients previously randomized to concentration-based dosing ($P=.38$). The rates of IBD-related hospitalization, abdominal surgery and steroid use were very low in patients with a durable treatment response to infliximab and significantly better than in

patients who had to discontinue infliximab (supplementary figure 1).

Serum infliximab levels and infliximab dosing in patients with a durable treatment response

In the patients on continued infliximab treatment at the end of follow-up, median trough concentrations were 4.73 µg/mL (IQR 3.30-6.42 µg/mL) and 108/167 (65%) patients had trough concentrations between 3-7 µg/mL.

Compared to the end of TAXIT maintenance phase, infliximab dosing had been intensified in 24/81 (29.6%) patients previously randomized to clinic-based dosing and in 32/86 (37.2%) patients previously randomized to concentration-based dosing ($P=.33$). De-intensification of infliximab dose had been done in 12/81 (14.8%) patients previously randomized to clinic-based dosing and in 15/86 (17.4%) patients previously randomized to concentration-based dosing ($P=.68$).

DISCUSSION

A very large proportion of CD and UC patients demonstrated mucosal healing at the end of TAXIT. Rates of mucosal healing were similar in the clinic-based dosing arm compared to the concentration-based dosing arm (91% vs. 90%). Currently, no universally accepted definition of mucosal healing exists, especially for CD. We defined mucosal healing as the absence of ulcerations or a clear improvement of ulcerations, as we felt this was the most clinical meaningful definition. When we re-analysed the results using complete mucosal healing (the absence of any ulcerations), the clinic-based dosing group had higher rates compared to concentration-based dosing group at the end of TAXIT. We cannot fully explain the discrepancy between both analyses except the fact the definition of complete mucosal healing resulted in a low number of patients with eligible endoscopy. Anyhow, proportion of patients with complete mucosal healing remained high in both groups, and the relative

difference between the clinic-based dosing group and the concentration-based dosing group was low (15%).

The STRIDE (Selecting Therapeutic Targets in Inflammatory Bowel Disease) consensus defined mucosal healing as one of the major treatment goals in patients with IBD.[11]

Mucosal healing is associated with sustained clinical remission, steroid-free remission, and reduced rates of hospitalization and surgery in CD.[12,13] In UC, studies demonstrated the association of mucosal healing with improved long-term clinical outcomes and reduced risk of colectomy. [14–17] We observed numerically lower healing rates at the end of TAXIT in patients who needed rescue therapy during maintenance phase of the trial, and the latter was more frequent in patients randomized to the clinic-based dosing arm. [7]

A previous reported trial showed that a high (68%) proportion of patients in clinical remission still has mucosal inflammation.[18] In a post-hoc analysis of SONIC trial only 53% of patients with a Crohn's Disease Activity Index (CDAI) < 150 had mucosal healing at week 26.[19] In our cohort, still 83% of patients without combined clinical and biochemical remission showed signs of mucosal healing on endoscopy. This can be due to the highly selected patient group of infliximab responders, with a long median disease duration (13.5 years), a long median time since the start of infliximab (5.6 years) and with only 10% of patients suffering of a flare-up in the prior 12 months. This limitation indeed makes it difficult to draw firm conclusions about the correlation between clinical and biochemical remission and mucosal healing. Also, the selection-bias might explain why there was no correlation between drug exposure during TAXIT maintenance phase and mucosal healing at the end of TAXIT, despite it is well established that anti-TNF serum trough concentrations correlate with (sustained) clinical response and remission and with mucosal healing in IBD [5,20–26].

During the long-term follow-up after TAXIT (median time of 41 months), durability of treatment response to infliximab was comparable between patients previously randomized to

the clinic-based dosing arm and patients previously randomized to the concentration-based dosing arm. In both groups, $\geq 75\%$ of patients continued infliximab, and drug concentrations in those patients remained fairly stable. This could be attributed to the proactive TDM that was applied in all patients. Indeed, every patient was dose optimised prior to TAXIT maintenance phase to target trough concentrations between 3-7 $\mu\text{g/mL}$, and 115/226 were randomized to the concentration-based dosing arm afterwards, with continued infliximab dosing based on trough concentrations for 1 extra year. Nevertheless, interpretation of the result remains difficult because of 2 reasons. First, a control group without TDM is missing. Second, this was a post-hoc analysis with every patient being treated in the same way after completion of TAXIT maintenance phase, with regular (approximately 1x/year proactively and supplementary in case of suspicion of loss of response) drug monitoring and dose adaptations if trough levels were not in the therapeutic interval of 3-7 $\mu\text{g/mL}$.

Infliximab discontinuation occurred earlier in patients previously randomized to clinic-based dosing than in patients randomized to concentration-based dosing ($P=.04$ for stop of infliximab because of all reasons, and $P=.15$ for stop of infliximab because of loss of response and/or immunogenicity). It has been shown that the development of ATI increases the probability of active disease even at low concentrations and in the presence of a therapeutic concentration of the drug.[27] In our cohort, 5 patients had detectable ATI using a drug sensitive assay 1 year after completion of TAXIT maintenance phase and all had been randomized before to the clinic-based dosing arm. These findings might support the use of proactive TDM monitoring, as in patients that continued infliximab, the rates of IBD-related hospitalization, abdominal surgery and steroid use during the entire follow-up period were very low and significantly better than in patients who had to discontinue infliximab. Nevertheless, it should be stressed that we did not observe a difference in long-term outcome between patients previously randomized to clinic-based dosing and patients previously

randomized to concentration-based dosing. These data are in line with those from the prospectively randomized Tailorix trial, where infliximab dose intensification based on a combination of symptoms and infliximab serum concentrations was not superior to dose intensification based on symptoms alone. [28] However, as increasing infliximab dose was possible based upon clinical symptoms alone regardless of the group a patient was randomized into, drawing firm conclusions out of Tailorix trial remains difficult. On the contrary, a recent large retrospective trial showed that proactive monitoring led to better clinical outcomes and lower risk of ATI formation in IBD patients treated with infliximab. [29]

ATI concentrations during long-term follow-up after TAXIT trial were only determined with a drug-sensitive assay. We recently reported results of a re-analysis of 222 serum samples collected during TAXIT trial, thereby measuring ATIs using a drug-tolerant assay. Low concentration ATIs, not detectable using a drug-sensitive assay, disappeared in more than half of the patients over time after dose optimization and were clinically non-relevant. [30]

Our study correlates clinical and biochemical data with endoscopic healing and trough concentrations and evaluates the effect of proactive TDM on the long-term outcome in a large cohort of IBD patients treated with infliximab. Follow-up was long and almost complete. Nevertheless, we recognize that there are several limitations. As stated before, we had a highly selected patient group of infliximab responders and all patients were treated according to routine clinical practice in our hospital after TAXIT, potentially influencing the long-term outcome. The study was retrospective. Endoscopy was not mandatory performed in all patients at the end of TAXIT. Even despite the rather large time frame to include eligible endoscopies at the end of TAXIT, still only 55% of patients could be reviewed. Furthermore,

endoscopies at the end of TAXIT were compared to baseline endoscopies (at the moment of diagnosis of IBD) and not with endoscopies at the start of TAXIT.

In conclusion, this retrospective analysis of TAXIT showed that the vast majority of patients demonstrated endoscopic mucosal healing at the end of TAXIT. Similar rates of mucosal healing were observed in patients after clinic-based dosing compared to concentration-based dosing. The co-primary endpoint of clinical and biochemical remission at the end of TAXIT maintenance phase correlated with mucosal healing. In the long-term follow-up after TAXIT, durability of response to infliximab was high but independent of previous randomization to either clinic-based or concentration-based dosing. Infliximab discontinuation occurred earlier in patients previously randomized to clinic-based dosing than to concentration-based dosing. Previous randomization to either clinic-based or concentration-based dosing did not influence outcome parameters in the long-term. More, prospectively collected, data are needed to establish the value of continued drug level measurement and adjustment of the therapeutic dose when needed during maintenance infliximab treatment.

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TABLES

Table 1: Baseline patient characteristics at the end of TAXIT maintenance phase

Characteristics	Total (n=226)	Clinic-based dosing arm (n=111)	Concentration-based dosing arm (n=115)	p-value
Male sex, n (%)	125 (55)	67 (60)	58 (50)	.143
Age, y, median (IQR)	41 (30-49)	41 (31-48)	41 (30-50)	.903
CD, n (%)	155 (69)	73 (66)	82 (71)	.393
Disease duration, y, median (IQR)	13.5 (7.3-20.8)	13.3 (8.0-19.0)	14 (6.8-21.5)	.882
Time since start infliximab, y, median (IQR)	5.6 (3.2-8.5)	5.5 (3.2-7.9)	5.7 (3.0-8.8)	.621
Concomitant IMM therapy, n (%)	9 (4)	4 (4)	5 (4)	1
Infliximab trough concentration, µg/mL, median (IQR)	5.18 (3.64-6.67)	5.21 (3.39-6.83)	5.04 (3.74-6.35)	.938
ATI, n (%)	3 (1)	3 (3)	0 (0)	.117
Flare up in past 12 months, n (%)	23 (10)	18 (16)	5 (4)	.004
Remission ^o , n (%)	158 (70)	77 (70)	81 (70)	.886

CD: Crohn's disease; IMM: immunomodulation therapy

^o Defined as Harvey-Bradshaw Index < 5 (Crohn's disease) or Partial Mayo Score < 3 (no individual subscore of >1) (ulcerative colitis) AND C-reactive protein ≤ 5.0 mg/L

Table 2: Characteristics of patients with eligible endoscopy at the end of TAXIT maintenance phase

Characteristics	Total (n=125)	Clinic-based dosing arm (n=55)	Concentration-based dosing arm (n=70)	p-value
Male sex, n (%)	70 (56)	32 (58)	38 (54)	.719
Age, y, median (IQR)	42 (32-51)	43 (34-49)	41 (32-52)	.676
CD, n (%)	90 (72)	38 (69)	52 (74)	.552
Concomitant IMM therapy, n (%)	7 (6)	4 (7)	3 (4)	.698
Flare-up in past 12 months, n (%)	12 (10)	10 (18)	2 (3)	.005
Remission ^o , n (%)	84 (67)	36 (65)	48 (69)	.848

CD: Crohn's disease; IMM: immunomodulation therapy

^o Defined as Harvey-Bradshaw Index < 5 (Crohn's disease) or Partial Mayo Score < 3 (no individual subscore of > 1) (ulcerative colitis) AND C-reactive protein ≤ 5.0 mg/L

Table 3: Reasons to stop infliximab

Reasons to stop infliximab	Number of patients (n=48)
Loss of response	14
Pharmacodynamic failure ¹	11
Pharmacokinetic failure ²	2
Immune-mediated failure ³	1
Immunogenicity (without loss of response)	7
Adverse events	18
Anaphylactic reaction	1
Arthralgia	3
Repeated infections	2
Skin reactions	9
Subjective intolerance	3
Other	9
Cancer (breast, pancreas)	2
Patient preference	2
Pregnancy (third trimester)	1
Surgery	2
Transplantation (kidney)	1
Wound problem	1

¹ Loss of response with normal drug concentrations and nondetectable antidrug antibodies; ² Loss of response with decreased drug levels and nondetectable antidrug antibodies; ³ Loss of response with decreased drug levels and detectable antidrug antibodies

FIGURES

Figure 1: Flow diagram showing mucosal healing at the end of TAXIT maintenance phase, compared by treatment arm.

CD: Crohn's disease; MH: mucosal healing; UC: ulcerative colitis

Figure 2: Kaplan-Meier curve of the time to stop infliximab after completion of TAXIT maintenance phase, compared by previous treatment arm during TAXIT maintenance phase.

IFX: infliximab

SUPPLEMENTARY FILE

Figure 1: Outcome parameters after TAXIT in patients who continued infliximab versus patients who discontinued infliximab.

IFX: infliximab

ACCEPTED MANUSCRIPT

Figure 1

Figure 2

Supplementary figure 1