Infliximab Exposure Associates With Radiologic Evidence of Healing in Patients With Crohn's Disease

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BACKGROUND & AIMS: **Higher infliximab trough levels are associated with clinical and endoscopic remission in patients with Crohn's disease (CD). We investigated pharmacodynamic features of infliximab and radiological healing.**

METHODS: **We performed a substudy of the TAILORIX trial (patients with active luminal CD in Europe, treated with infliximab), analyzing baseline and week 54 magnetic resonance enterography (MRE) data. MREs were scored using the MaRIA score by blinded central readers. Radiologic response and remission were defined, based on MaRIA criteria in all segments, as scores below 11 and 7, respectively. We collected data on infliximab trough levels, biomarkers, and endoscopic endoscopy findings. Our primary aim was to evaluate pharmacodynamic features associated with radiologic response and remission, based on MRE assessments at baseline and at 54 weeks after initiation of infliximab therapy.**

RESULTS: **We analyzed data from 36 patients (50% female; median age 35.7 years; interquartile age range, 25.6–48.6 years; median disease duration, 1.5 months; interquartile duration range, 0.6–22.4 months). At week 54 of treatment, 36.4% of patients had a radiologic response, 30.3% of patients were in remission, and 71% had endoscopic features of remission. At baseline, there was a correlation between the CD endoscopic index of severity and MaRIA scores (κ = 0.46; P = .008), but we found no correlation at week 54 (κ = 0.06; P =. 75). Radiologic remission correlated with infliximab trough level at week 14 (P = .049) when the infliximab trough level cut-off value was set at 7.8 μg/ml (area under the curve, 0.74; 75% sensitivity; 86% specificity; 90% negative predictive value; 57% positive predictive value). Radiologic response correlated with infliximab trough levels at week 14 (P = .048) when the infliximab trough level cut-off value was set at 7.8 μg/ml (area under the curve, 0.73; 70% sensitivity; 90% specificity; 86% negative**

Abbreviations used in this paper: CD, Crohn's disease; CDEIS, Crohn's Disease Endoscopic Index of Severity; CR, central reader; FISP, fast imaging with steady-state precession; ICC, intraclass correlation; IQR, interquartile range; MaRIA, Magnetic Resonance Index of Activity; MRE, magnetic resonance enterography; PEG, polyethylene glycol; ROC, receiver operating characteristics; TAILORIX, randomized controlled trial investigating tailored treatment with infliximab for active luminal Crohn's disease.

1542-3565/$36.00
https://doi.org/10.1016/j.cgh.2020.04.052

predictive value; 78% positive predictive value) and with continuous pharmacologic evidence of response (infliximab trough levels above 5.0 μg/ml at all time points) (P = .034).

CONCLUSIONS: **In a substudy of data from the TAILORIX trial of patients with active luminal CD, we identified a relationship between exposure to infliximab and radiologic evidence of outcomes.**

Keywords: Biomarker; Prognostic Factor; Anti-TNF Agent; Response to Therapy; TAILORIX.

Crohn's disease (CD) is an inflammatory disease that affects the gastrointestinal tract over a variable extent. The major clinical characteristic that discriminates CD from ulcerative colitis is the transmural nature of the inflammation.[1] The current gold standard to assess disease activity in CD is endoscopy.[2] The regression of intraluminal lesions (ie, endoscopic remission) is associated with favorable long-term outcomes in CD.[3] During the last decades newer modalities to assess also this transmural aspect of disease activity in CD emerged.[4] Magnetic resonance enterography (MRE) provides an assessment of the luminal, mural, and extraluminal manifestation of CD. Disease activity scores have been developed to systematically assess the severity of inflammation on MRE.[5,6] It has been documented that as early as week 2 after the start of infliximab, improvement in disease activity based on MRE can be detected.[7] Only a minority of patients achieve complete disappearance of inflammatory lesions on MRE during maintenance therapy with infliximab.[7] Radiologic response has also been associated with better outcomes in CD patients, and recent evidence suggests that radiologic healing might be the ultimate therapeutic goal in CD.[8–11] It is well-established that there is a clear exposure-response relationship for infliximab, with higher infliximab trough levels being associated with endoscopic remission.[12] Currently no data are available on the effect of infliximab on radiologic remission in patients with CD.

Therefore the aim of this study was to evaluate the pharmacodynamics of infliximab in radiologic response and remission in patients with CD on the basis of MRE assessments at baseline and at 54 weeks after initiation of infliximab therapy by using the data of the TAILORIX study.[13]

Methods

Patient Population

The multicenter (27 centers in Belgium, France, and the Netherlands) randomized controlled trial investigating tailored treatment with infliximab for active luminal Crohn's disease TAILORIX aimed to explore the role of tailored treatment with infliximab in biological naive patients with active luminal CD.[13] In total, 167 patients were screened, and 122 patients with moderate to severely active CD (Crohn's disease activity index 220–450) were started on infliximab in combination with an immunomodulator. Patients were randomized at week 14 after standard induction regimen (infliximab 5 mg/kg week 0-2-6) to receive 1 of 3 regimens of monitoring-based dosage adjustments, on the basis of clinical symptoms only or on a combination of clinical symptoms, C-reactive protein levels, fecal calprotectin levels, and infliximab trough levels.

At weeks 0, 12, and 54, patients underwent a prescheduled ileocolonoscopy. The endoscopic activity of disease was scored blindly on the basis of the Crohn's Disease Endoscopic Index of Severity (CDEIS).[14] MREs were performed in a priori selected centers (n = 5). Selection was based on ability to perform high quality MRE and recruitment potential. Patients consented separately to participate in the MRE substudy. These patients (representing >50% of the total number of included patients per selected site) underwent an MRE at week 0 and week 54 or at the early termination visit. For the current analysis all patients with at least 1 MRE in the TAILORIX study were included, irrespective of treatment group to which the patients were assigned in the study. Clinical, biochemical, endoscopic, and pharmacologic data from the TAILORIX trial were available for these patients.

Magnetic Resonance Imaging Methodology

MRE was performed in 5 of the 27 participating centers. The MRE was preferentially performed on the same day as the ileocolonoscopy. The patient had nil per mouth on the day of the examination. Forty-five minutes before the MRE the patient ingested ≈1500 mL polyethylene glycol (PEG) 4000 (or 3350), with additional oral ingestion of 500 mL water or PEG 15 minutes before examination. At the start of the examination 0.5 mg glucagon was administrated intravenously just before intravenous injection of gadolinium. The patient was placed in procubitus position with a phased array body coil. The following sequences were performed: coronal and axial true fast imaging with steady-state precession (true FISP) sequence, with breath hold, without fat suppressed, and with a slice thickness of 5 mm and a skip of 0 mm; coronal true FISP sequence, with breath hold, with fat suppression, and with a slice thickness of 5 mm and a skip of 0 mm; coronal and axial T2 weighted images using single shot fast spin echo sequence with a slice thickness of 5 mm and a skip of 0 mm; and coronal 3-dimensional T1-weighted gradient echo sequence with

breath hold with a slice thickness of 2–3 mm. Sixty seconds after injection of gadolinium (0.1 mmol/kg), coronal and axial gadolinium enhanced 3-dimensional gradient echo sequence with breath hold, with a slice thickness of 2–3 mm was acquired. Axial 2-dimensional T1-weighted gradient echo sequence after injection of gadolinium with a slice thickness of 5 mm and a skip of 0 mm was acquired. The images were archived on a Data on Picture Archiving and Communication System and compact disk.

Magnetic Resonance Enterography Central Reading

All MRE images were de-identified. The MRE studies were centrally reviewed by 6 different central readers (CRs) as prespecified in the protocol; all of them had more than 10 years of experience in abdominal imaging. The MRE studies were assigned randomly to the different CRs. Every CR was blinded to patient data and clinical information. Every CR scored ≈24 MRE studies randomly; in this way all MREs were randomly scored twice by 2 different CRs. The MREs were scored by using the Magnetic Resonance Index of Activity (MaRIA).[5] The MaRIA index was calculated by using the previously published formula: 1.5 × wall thickening (mm) + 0.02 × RCE (relative contrast enhancement) + 5 × edema + 10 × ulcers.[5,15] Global MaRIA score is based on terminal ileum and all colonic segments. For the calculation of the MaRIA index an electronic clinical research form was used that automatically calculated the score. The threshold for discrepancy between 2 readers was set at a difference of 1.5 points in the MaRIA index per segment, if active disease was present (MaRIA ≥7 in at least 1 segment). If there was a discrepancy between 2 CRs in at least 1 segment (independent of any discrepancy in the global MaRIA index), then the images were adjudicated by a third independent CR (JR). In case no adjudication was needed, then the mean of the scores of the 2 CRs was used. The global MaRIA was the sum of the mean scores per segment (in case no adjudication was needed) and/or the adjudicated scores per segment. Global radiologic response and remission were defined as MaRIA score in all segments <11 and <7, respectively, in patients with active radiologic disease at baseline. Segmental radiologic response and remission were defined as MaRIA score in one segment <11 and <7, respectively.[16]

Statistical Analysis

Statistical analysis was done by using SPSS 26.0 (IBM Corp, Armonk, NY) and Graphpad Prism 5.01 (GraphPad Software, San Diego, CA). Continuous variables with non-normal distribution are described as medians with interquartile range (IQR). Categorical variables are described as percentages. For time independent evaluation of continuous variables we used the Mann-Whitney test, and for categorical variables we used the χ^2 tests (univariate analysis). Correlation with outcomes was based on patients with radiologic active disease at baseline (extrapolated for missing MRE baseline) and available MRE at week 54 (n = 31). The Wilcoxon signed-rank test was performed to test differences between 2 measurements at different time points in the same patient. Intraclass correlation (ICC) (2-way random model and absolute agreement type) was used to test the inter-rater reliability of a continuous score (MaRIA score).[17] For this we categorized the continuous values (severe partial MaRIA ≥11; active partial MaRIA <11; inactive partial MaRIA <7). Results of ICC analysis were classified as very good (coefficients, 0.81–1.00), good (0.61–0.80), moderate (0.41–0.60), fair (0.21–0.40), and poor (<0.21). Two-tailed P value <.05 is considered as statistically significant. No correction for multiple testing was applied. Receiver operating characteristics (ROC) curves were used to determine cutoff values of continuous variables.

What You Need to Know

Background

Increased exposure to infliximab results in higher rates of endoscopic healing in patients with Crohn's disease (CD). Radiologic remission, determined by magnetic resonance enterography, associates with long-term outcomes but is difficult to achieve.

Findings

Radiologic remission was achieved in approximately one-third of patients with luminal CD treated with infliximab. An infliximab trough level of 7.8 μg/mL at the end of induction therapy was associated with radiologic response and remission.

Implications for patient care

Radiologic healing is difficult but achievable for patients with luminal CD. Monitoring trough levels of infliximab can guide treatment, and optimizing dosing during induction therapy could improve long-term outcomes.

Results

Patient Population

In total, 36 of the 122 patients (30%) in the TAILORIX trial had at least 1 MRE. The majority (31/36) had both a baseline and week 54 MRE; these patients were analyzed in the PD analysis to assess correlation between drug exposure and outcomes over time. Two patients had no baseline MRE, 2 patients had an MRE at the moment of early termination (week 26 and week 32, respectively), and 1 patient had no week 54 MRE. The patient

Table 1. Patient Characteristics of Patients Included in TAILORIX Trial With at Least 1 MRE and Total Evaluable TAILORIX Cohort[12] and Infliximab Exposure Data of MRE Cohort

	MRE TAILORIX cohort, n = 36	Total TAILORIX cohort, n = 116[12]
Median age (IQR), *y*	35.7 (25.6–48.6)	30 (22–45)
Median disease duration (IQR), *mo*	1.5 (0.6–22.4)	7 (1–78)
Gender distribution (M/F)	18/18	58/68
Median baseline C-reactive protein (IQR), *mg/L*	22 (7.8–34.3)	20.0 (9.0–36.5)
Median baseline fecal calprotectin (IQR), *μg/g*	1501 (780–1800)	1462.5 (726–1800)
Median CDAI (IQR)	282 (246–321)	280 (236–321)
Dosing regimen[13] (%)	Dosing regimen 1: 39 Dosing regimen 2: 33 Control group: 27.8	Dosing regimen 1: 36.9 Dosing regimen 2: 30.3 Control group: 32.8
Median yearly infliximab dose per body weight (only in patients reaching week 54) (IQR), *mg/kg/y*	55.31 (44.9–67.8)	
Median infliximab trough level week 14 (IQR), *μg/mL*	5.8 (3–8)	
Median infliximab trough level week 54 (IQR), *μg/mL*	6.5 (4–11)	
Infliximab trough levels >2 μg/mL at any time point (%)	24/36 (67)	
Infliximab trough levels >3 μg/mL at any time point (%)	19/36 (53)	
Infliximab trough levels >5 μg/mL at any time point (%)	9/36 (25)	
Infliximab trough levels >7 μg/mL at any time point (%)	4/36 (11)	
Need for dose adjustment (%)	21/36 (58)	

CDAI, Crohn's disease activity index; IQR, interquartile range; MRE, magnetic resonance enterography; TAILORIX, randomized controlled trial investigating tailored treatment with infliximab for active luminal Crohn's disease.

characteristics are presented in Table 1. As per inclusion criteria of the TAILORIX trial, all patients had moderate to severely active CD and active endoscopic lesions at baseline.

Magnetic Resonance Enterography Results

From the 69 MREs included in the study, in total 53 MREs had discrepancy between the 2 CRs in at least 1 segment based on the prior established threshold. A total of 123 segments (123/414, 29.7%) therefore needed adjudication. Of these segments 53% had inactive disease, and 47% had active disease of which 60% had severe disease. The ileal (n = 27, 63% active disease) and the sigmoidal segments (n = 28, 68% inactive disease) needed most adjudications. There was no difference in the number of studies with discrepancy between baseline (n = 27) and week 54 (n = 24). Overall, on the basis of the ICC analysis the reliability of the scoring of the different readers was moderate to good at baseline.

Table 2. Intraclass Correlation Between the 2 Random Readers

Segment	Week 0	Week 54
Ileum	0.746 ($P < .0001$)	0.671 ($P = .002$)
Ascending colon	0.792 ($P < .0001$)	0.249 ($P = .231$)
Transverse colon	0.751 ($P < .0001$)	0.434 ($P = .076$)
Descending colon	0.514 ($P = .021$)	0.177 ($P = .311$)
Sigmoid colon	0.602 ($P = .004$)	–0.133 ($P = .626$)
Rectum	0.726 ($P = .001$)	0.688 ($P = .002$)

NOTE. Results of ICC analysis were classified as very good (coefficients, 0.81–1.00), good (0.61–0.80), moderate (0.41–0.60), fair (0.21–0.40), and poor (<0.21).

At week 54 the correlation was only good in the ileum and rectum (Table 2).

The radiologic response and remission rate at week 54 were 36.4% and 30.3%, respectively. The results of the final MaRIA scores per segment are shown in Supplementary Figure 1*A* and *B*. There was a significant decrease in the median global MaRIA score from baseline to the end of the study from 53 (IQR, 42–73) to 43 (IQR, 28–53) ($P = .001$).

In patients with active disease at baseline, the segmental radiologic remission rate in the ileum was only 25%. The segmental radiologic remission rates were higher in the colonic segments (70% ascending, 80% transverse, 87% descending, 75% sigmoid, and 44% rectum) (Supplementary Figure 1*C*). In all segments apart from the rectum there was a significant decrease in median segmental MaRIA score at week 54 compared with baseline.

Correlation Between Radiology and Endoscopy

Endoscopic remission (CDEIS <3) was achieved in a much higher proportion of patients (71%) than radiologic remission. There was a correlation between the global MaRIA and the CDEIS (continuous variables) at baseline ($\kappa = 0.46$; $P = .008$). At week 54 no correlation was seen between the CDEIS and the global MaRIA score ($\kappa = 0.06$; $P = .75$). The reason for the absence of any correlation at week 54 was the floor phenomenon that was seen in patients with endoscopic remission (CDEIS <3) who still had high MaRIA scores (Figure 1). When correlating endoscopic and radiologic remission (categorical variables) in patients at week 54, no association was seen when using either CDEIS <3 ($P = .107$) or CDEIS <4 ($P = .06$) as definition of endoscopic remission.

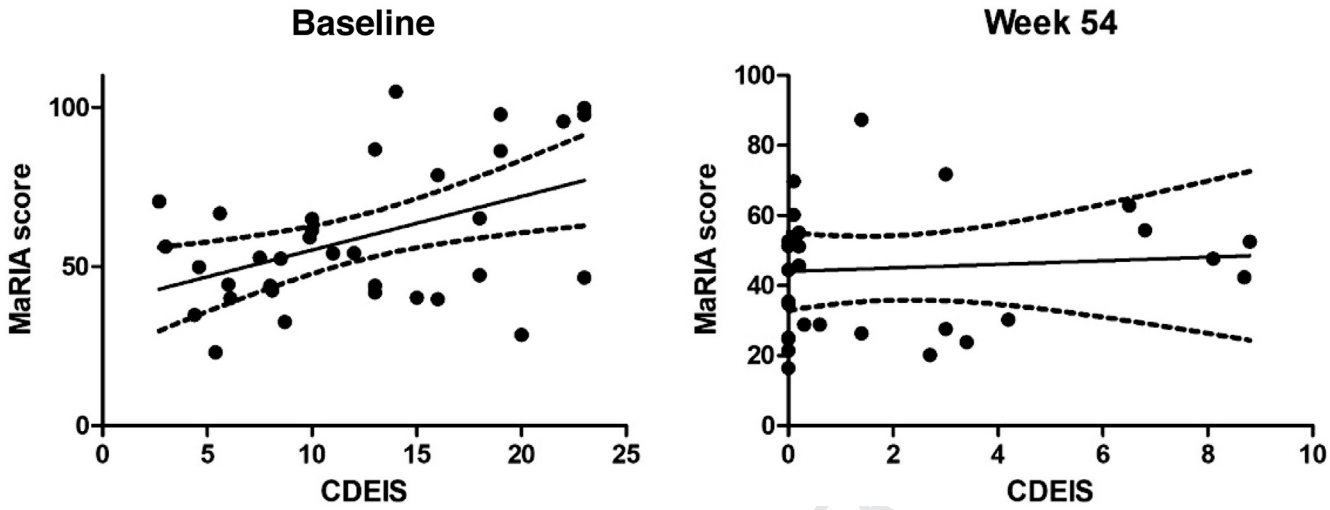

Figure 1. Correlation between the CDEIS and MaRIA score at baseline ($\kappa = 0.46$; $P = .008$) and week 54 ($\kappa = 0.06$; $P = .75$); trend line (*full line*), 95% confidence interval (*dotted line*). CDEIS, Crohn's Disease Endoscopic Index of Severity; MaRIA, Magnetic Resonance Index of Activity.

Pharmacodynamics of Infliximab and Radiologic Response and Remission

Radiologic remission at week 54 was correlated with infliximab trough levels at week 14 ($P = .049$). On the basis of a ROC analysis infliximab trough level value of 7.8 μg/mL at week 14 was identified as cutoff to predict radiologic remission over time (area under the curve 0.74; sensitivity 75%; specificity 86%; negative predictive value 90%; and positive predictive value 67%) (Figure 2*A*). Radiologic response at week 54 was correlated with infliximab trough levels at week 14 ($P = .048$) and with continuous pharmacologic response (infliximab trough levels >5.0 μg/mL at all time points) ($P = .034$). An ROC-based infliximab trough level cutoff value of 7.8 μg/mL was identified (area under the curve 0.73; sensitivity 70%; specificity 90%; negative predictive value 86%; and positive predictive value 78%) for being predictive for radiologic response (Figure 2*B*). There was a numerically but not statistically significant difference

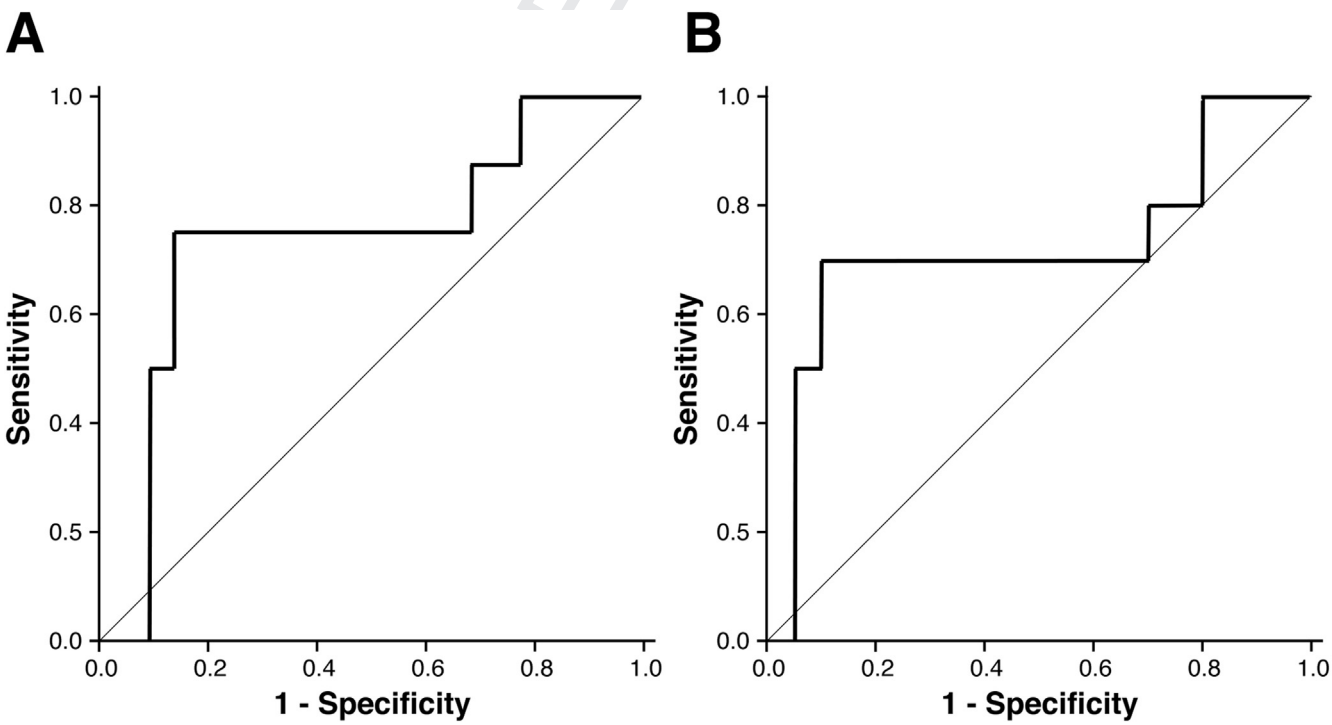

Figure 2. Receiver operating characteristics curve indicating infliximab trough level cutoff value of 7.8 μg/mL at week 14 being associated with (*A*) radiologic remission at week 54 (area under the curve 0.74; sensitivity 75%; and specificity 86%; negative predictive value 90% and positive predictive value 67%); (*B*) with radiologic response at week 54 (area under the curve 0.73; sensitivity 70%; and specificity 90%; negative predictive value 86% and positive predictive value 78%).

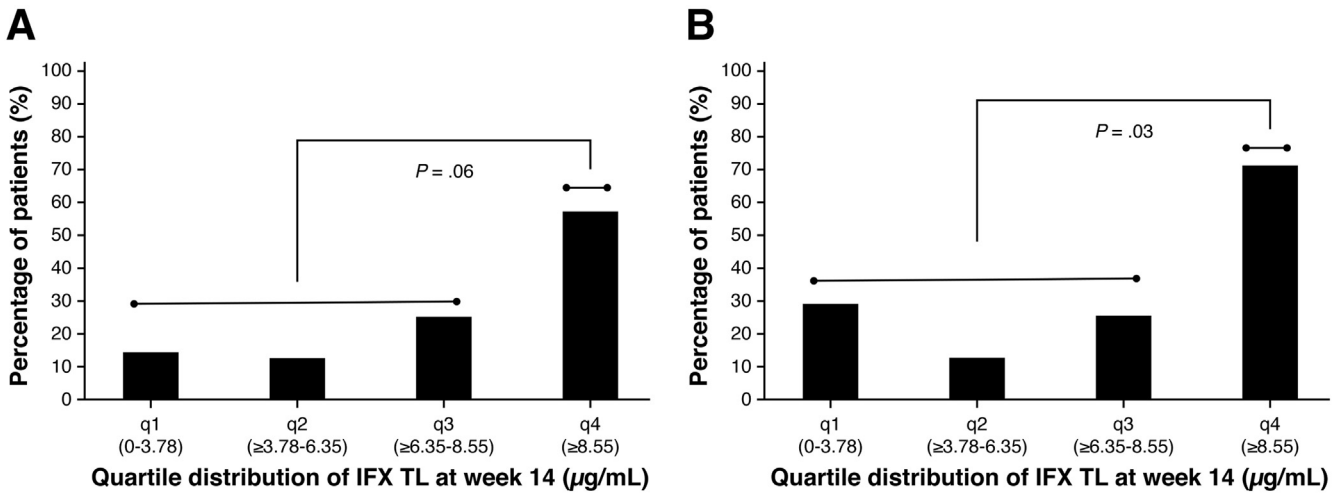

Figure 3. Radiologic remission (*A*) and response (*B*) at week 54 per infliximab (IFX) trough level (TL) quartile at week 14. Significantly higher radiologic response rate for the highest quartile ($P = .03$).

in infliximab trough levels at week 54 among patients with or without radiologic remission ($P = .13$) (Supplementary Figure 2). When looking at the infliximab trough levels per quartile at week 14, patients in the highest quartile had the highest radiologic response ($P = .03$) and remission ($P = .06$) rate at week 54 (Figure 3). Comparing patients with both endoscopic and radiologic remission (median infliximab trough level, 8.5; IQR, 4.6–10.4) with patients with only endoscopic remission (median infliximab trough level, 5.8; IQR, 2.7–6.5), a numeric but no statistically significant difference was seen in the infliximab trough levels at week 14 ($P = .095$); no difference was seen at week 54 ($P = .35$). A subgroup of 21 patients had dose escalation during maintenance therapy with infliximab. In this subgroup continuous pharmacologic response (infliximab >7 μg/mL at all time points) was associated with radiologic response ($P = .039$) and remission ($P = .019$). No difference was seen in the radiologic remission ($P = .59$) or response ($P = .76$) rates comparing patients with or without dose adjustments during maintenance.

Discussion

This substudy of the prospective TAILORIX study shows that radiologic remission and response can be achieved with infliximab in patients with early luminal CD, although to a much lower extent than endoscopic remission. Infliximab trough level of 7.8 μg/mL at the end of induction (week 14) was associated with both endoscopic response and remission. A continuous high infliximab exposure (infliximab >5 μg/mL at all time points) was associated with radiologic response. This study confirms the exposure-response relationship of infliximab for radiologic remission. Previously an observational cross-sectional study showed association between adalimumab levels and bowel wall thickness based on intestinal ultrasound.[18] Several studies have shown the exposure-response relationship for infliximab with endoscopic remission. A post hoc analysis of the Active Ulcerative Colitis Trials 1 and 2 showed that infliximab levels of 5.1 μg/mL and 6.7 μg/mL at week 14 were associated with endoscopic improvement and remission at week 30, respectively.[19] Also infliximab maintenance trough levels ≥7.5 μg/mL are associated with long-term endoscopic response in ulcerative colitis.[20] Although proactive therapeutic drug monitoring is not supported by robust evidence at this stage,[12,13,21–23] our results do suggest that optimal induction dosing could improve the outcomes of the patient. Moreover, in patients with dose adjustments maintenance infliximab trough levels >7 μg/mL were associated with radiologic remission. Because radiologic remission is more difficult to achieve than endoscopic remission, higher drug exposure might be needed to reach this target.

At baseline there was a correlation between the endoscopic and radiologic disease activity that is in line with prior observations for MaRIA and other MRE scores.[24] However, at week 54 there was a striking disconnect between endoscopic and radiologic remission, suggesting that radiologic remission is a more difficult target to reach. Less than half of the patients with endoscopic remission achieved radiologic remission. Data suggest that radiologic healing implies favorable clinical long-term outcomes.[8–10] Although it might be difficult to discriminate chronic bowel damage from active disease on MRE,[25] this is not applicable to our cohort. With a median disease duration of 1.5 months we do not expect a high burden of bowel damage. Other studies showed better correlation between endoscopic and radiologic remission. In the original development cohort of the MaRIA score an optimal correlation was seen between MaRIA and CDEIS ($r = 0.82$, $P < .001$), but 74% of this cohort had active endoscopic disease. Furthermore, the scoring methodology was not the same in the original MaRIA article compared with the methodology used in the current study (different CDEIS

calculation, blinding of the endoscopist, number of radiologists involved). Better correlation is also seen when using less robust scoring of radiologic remission such as in the pediatric ImageKids study,[26] in which the definition of radiologic remission was based on a visual analogue scale indicating the radiologist global assessment. In this study there was a match of endoscopic and radiologic remission in 69% of the patients, and only a minority of the patients had persisting radiologic signs of disease activity in absence of endoscopic lesions (6%). Efforts have been made to minimize the limitations of the current MaRIA score, leading to a more simplified version that correlates strongly with the CDEIS.[27] Of note, there is clear difference in radiologic healing rate according to the location of the disease. Colonic segments have higher radiologic healing rates than the active disease located in the ileum. These findings are in line with what is seen in this cohort on an endoscopic level (unpublished data, Riviere et al, UEGW 2019).

Our study has several strengths. First, a robust methodology for the central reading of the MREs was applied, with random allocation of the MREs to 6 experienced radiologists. A low threshold was set for the need for adjudication, resulting in an optimal scoring. Second, this is a unique cohort of patients with prospectively collected clinical, pharmacologic, endoscopic, and radiologic data. Our study also has some limitations. The patient cohort was relatively small, with only 36 patients included of which 31 had baseline and week 54 MRE; however, this is counterbalanced by the fact that we used objective endpoints such as the infliximab trough levels and radiologic healing in luminal CD. Of note, different dose adjustment regimens were possible in the TAILORIX trial. However, in this study all patients had an identical induction regimen with infliximab. Furthermore, we focused not on the dosing as such but on the effective drug exposure based on the infliximab trough levels. Third, MREs were performed on the different MR systems with variable performance. This could indeed influence the quality of the scoring and the inter-rater variability. In addition, it is striking that the inter-rater variability was mainly high in the colonic segments. That can be explained by poorer performance of radiologic scoring in the colon compared with the ileum. By using a stringent protocol for the imaging and a balanced central reading methodology, we could minimize the impact of this variance. One could argue that the correlation between endoscopic and radiologic disease activity might be better when applying more thorough CR training and optimizing the MRE sequences, in particular T2-fat saturation. Finally, we found no significant association between the infliximab trough level at week 14 and the endoscopic outcome. This comparison between the target trough levels for the different outcomes is not possible.

In conclusion, this prospective study indicates the exposure-response relationship for infliximab for radiologic response and remission in luminal CD. Adequate infliximab trough levels at the end of induction are associated with beneficial radiologic outcomes at 1 year. The target of radiologic remission is achievable but to a lower extent compared with endoscopic remission.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at https://doi.org/10.1016/j.cgh.2020.04.052.

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Acknowledgments
The authors thank Sabrina Williams and Marie-Jo Bertin from the GETAID office for their support in organizing this study, all local investigators and study coordinators who helped with the patient recruitment and follow-up, and all the patients who participated in this study.

TAILORIX study group: Guy Lambrecht, Anthony Buisson, Yoram Bouhnik, Janneke Vander Woude, Philippe Van Hootegem, Jacques Moreau, Edouard Louis, Denis Franchimont, Martine De Vos, Fazia Mana, Hedia Brixi, Matthieu Allez, Philip Caenepeel, Alexandre Aubourg, Bas Oldenburg, Marieke Pierik, and Sylvie Chevret.

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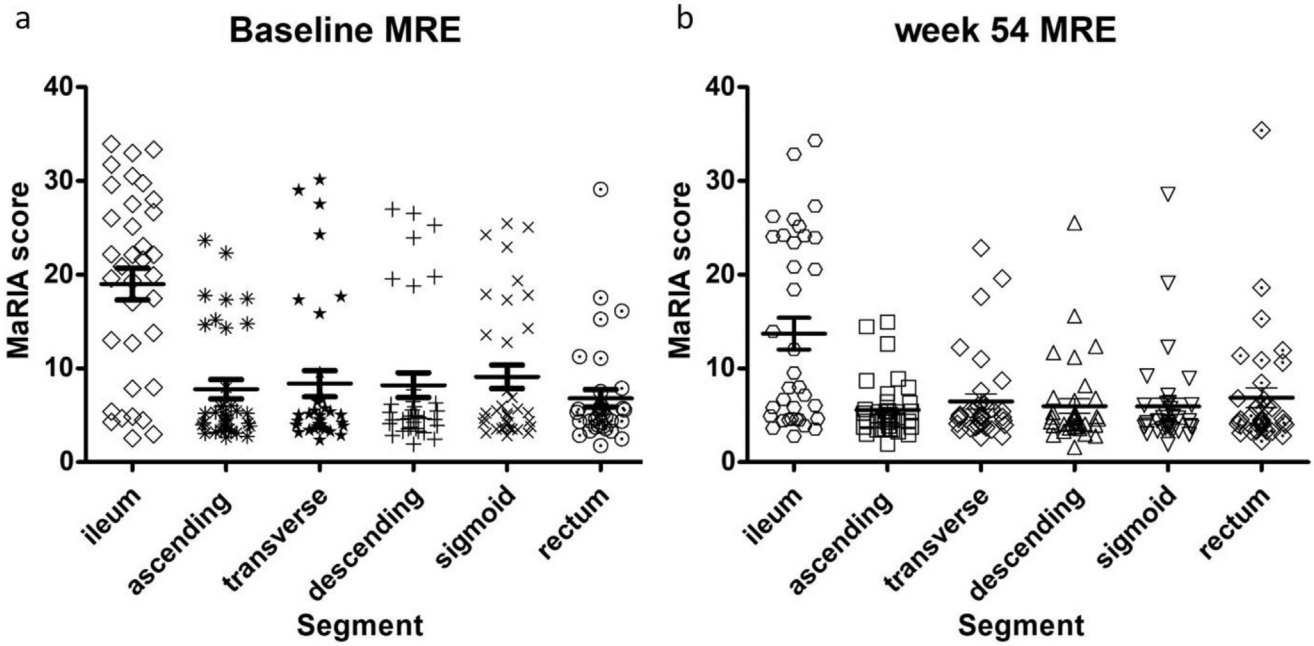
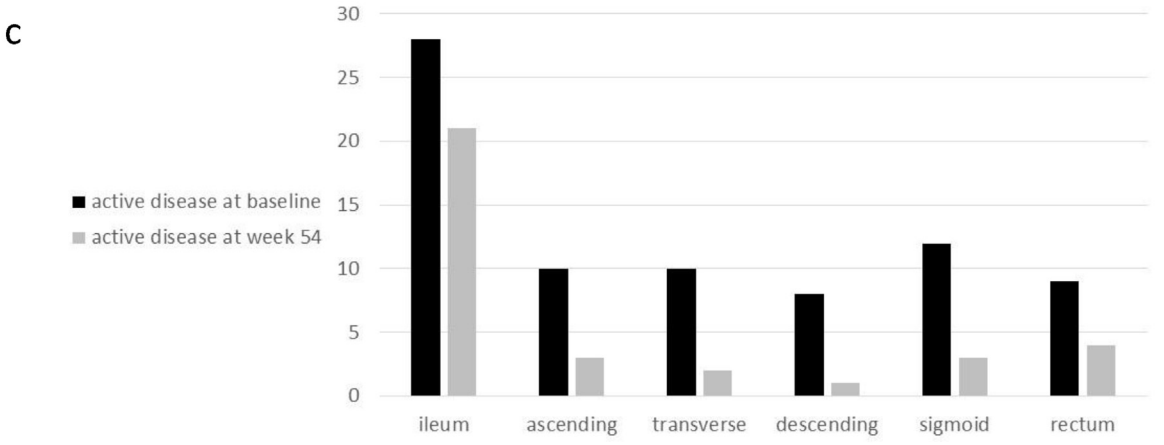
Conflicts of interest

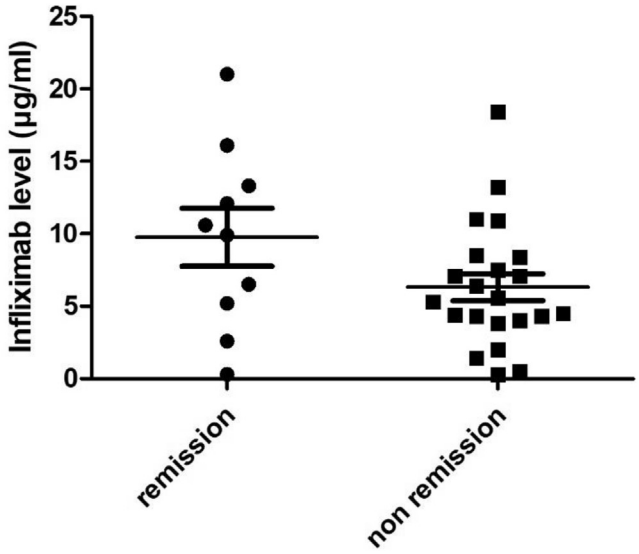
These authors disclose the following: PB has received financial support for research from AbbVie, Mundipharma, Pfizer, Janssen, and Mylan; lecture fees from AbbVie, Takeda, Pfizer, and Janssen; and advisory board fees from AbbVie, BMS, Takeda, Hospira, Janssen, MSD, Mundipharma, Roche, Pfizer, Sandoz, and Pentax. ED is a postdoctoral research fellow of the Research Foundation – Flanders (FWO), Belgium (grant number 12X9420N) and received consultancy fees from Janssen (all honoraria/fees paid to the department). MZ has received lecture fees from AbbVie. FB has received lectures and consultancy fees from AbbVie, Amgen Chiesi, Ipsen, MSD, and Roche; and consultancy fees from AbbVie, Celgene, Falk, Ferring, Janssen, Mundipharma, MSD, Norgine Pfizer, Takeda, and Vifor. GD has served as advisor for AbbVie, Ablynx, Allergan, Alphabiomics, Amakem, Amgen, AM Pharma, Applied Molecular Therapeutics, Arena Pharmaceuticals, AstraZeneca, Avaxia, Biogen, Bristol Meiers Squibb, Boehringer Ingelheim, Celgene/Receptos, Celltrion, Cosmo, DSM Pharma, Echo Pharmaceuticals, Eli Lilly, Engene, Exeliom Biosciences, Ferring, DrFALK Pharma, Galapagos, Genentech/Roche, Gilead, Glaxo Smith Kline, Gossamerbio, Hospira/Pfizer, Immunic, Johnson and Johnson, Kintai Therapeutics, Lycera, Medimetrics, Millenium/Takeda, Medtronics, Mitsubishi Pharma, Merck Sharp Dome, Mundipharma, Nextbiotics, Novonordisk, Otsuka, Pfizer/Hospira, Photopill, ProciseDx, Prodigest, Prometheus Laboratories/ Nestle, Progenity, Protagonist, RedHill, Robarts Clinical Trials, Salix, Samsung Bioepis, Sandoz, Seres/Nestle, Setpoint, Shire, Teva, Tigenix, Tillotts, Topivert, Versant, and Vifor; and received speaker fees from AbbVie, Biogen, Ferring, Johnson and Johnson, Merck Sharp Dome, Mundipharma, Norgine, Pfizer, Samsung Bioepis, Shire, Millenium/Takeda, Tillotts, and Vifor. DL has received advisory board or lectures fees from AbbVie, Celgene, Ferring, Janssen, MSD, Novartis, Pfizer, Roche, and Takeda. LPB has received personal fees from AbbVie, Janssen, Genentech, Ferring, Tillots, Pharmacosmos, Celltrion, Takeda, Boerhinger Ingelheim, Pfizer, Index Pharmaceuticals, Sandoz, Celgene, Biogen, Samsung Bioepis, Alma, Sterna, Nestle, Enterome, Allergan, MSD, Roche, Arena, Gilead, Hikma, Amgen; grants from AbbVie, MSD, and Takeda; and stock options from CTMA. SV has received financial support for research from MSD, AbbVie, Takeda, Pfizer, J&J; lecture fee(s) from MSD, AbbVie, Takeda, Ferring, Centocor, Hospira, Pfizer, J&J, and Genentech/ Roche; and consultancy fees from MSD, AbbVie, Takeda, Ferring, Centocor, Hospira, Pfizer, J&J, Genentech/Roche, Celgene, Mundipharma, Celltrion, SecondGenome, Prometheus, Shire, Prodigest, Gilead, Galapagos, and MRM Health. The remaining authors disclose no conflicts.





Radiological active disease at baseline (n)	28	10	10	8	12	9
Radiological active disease at week 54 (n)	21	3	2	1	3	4
Median MaRIA w0 (IQR)	22 (18-29)	16 (15-19)	21 (16-29)	22 (19-26)	18 (14-24)	13 (9-17)
Median MaRIA w54 (IQR)	18 (7-24)	5 (4-8)	5 (5-16)	5 (4-6)	5 (4-7)	9 (5-17)

Supplementary Figure 1. Evolution of radiologic activity over time. (*A*) Box plot of segmental MaRIA score at baseline, (*B*) box plot of segmental MaRIA score at week 54 (*1 dot* per patient, *bars* = mean with standard error of the mean), (*C*) evolution of number of patients with active disease per segment (MaRIA score $\geq$7), and evolution in median segmental MaRIA score from baseline to week 54 in patients with active segmental disease (decrease all $P < .02$, except rectum $P = .16$). IQR, interquartile range; MaRIA, Magnetic Resonance Index of Activity; MRE, magnetic resonance enterography.



Supplementary Figure 2. Infliximab trough level at week 54 in patients with and without radiologic remission at week 54 ($P = .13$) (*1 dot* per patient, *bars* = mean with standard error of the mean).