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Adalimumab in Biologic-naïve Patients With Crohn's Disease After Resolution of an Intra-abdominal Abscess: A Prospective Study From the GETAID

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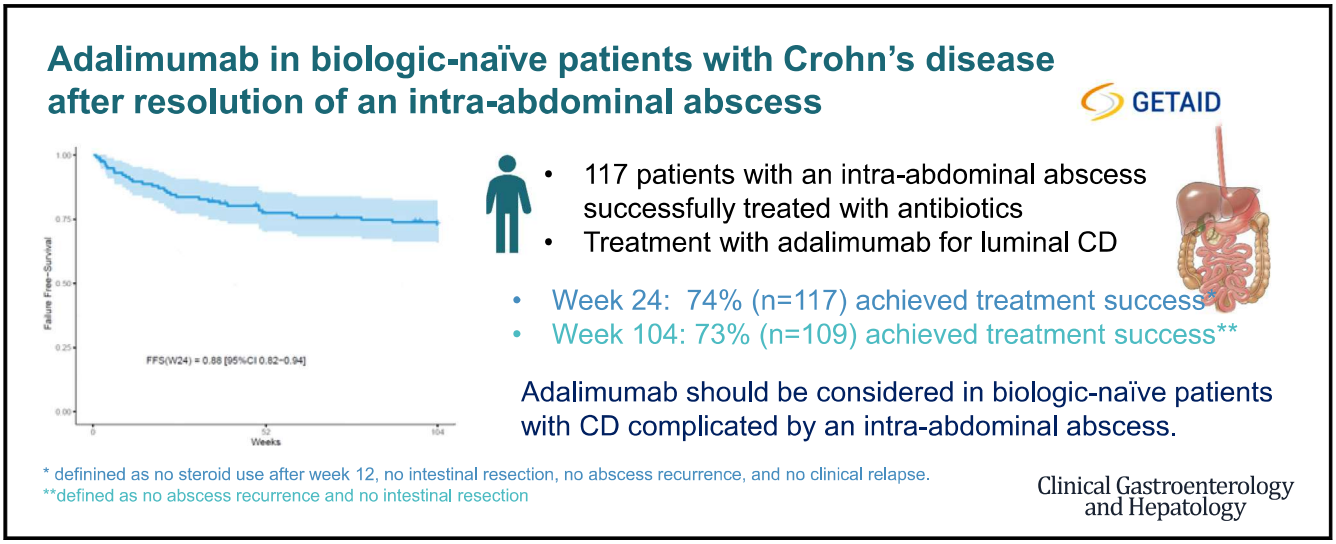

Abbreviations used in this paper: **AE, adverse event; CD, Crohn's disease; CDAI, Crohn's Disease Activity Index; CDOS, Crohn's Disease Obstructive Score; CI, confidence interval; CRP, C-reactive protein; CT, computed tomography; GETAID, Groupe d'Etudes Thérapeutiques des Affections Inflammatoires du Tube Digestif; HR, hazard ratio; IBD, inflammatory bowel disease; IQR, interquartile range; MRE, magnetic resonance enterography; OR, odds ratio; SAE, serious adverse event; W, week.**

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BACKGROUND & AIMS: **The management of intra-abdominal abscesses complicating Crohn's disease (CD) is challenging, and surgery with delayed intestinal resection is often recommended. The aims of this study were to estimate the success rate of adalimumab (ADA) in patients with CD with an intra-abdominal abscess resolved without surgery, and to identify predictive factors for success.**

METHODS: **A multicenter, prospective study was conducted in biologic-naïve patients with CD with resolved intra-abdominal abscess treated with ADA with a 2-year follow-up. The primary endpoint was ADA failure at week (W) 24 defined as a need for steroids after W12, intestinal resection, abscess recurrence, and clinical relapse. Secondary post-hoc endpoint was the long-term success defined as the survival without abscess relapse or intestinal resection at W104. The factors associated with ADA failure at W24 and W104 were identified using a logistic and a Cox regression, respectively.**

RESULTS: **From April 2013 to December 2017, 190 patients from 27 GETAID centers were screened, and 117 were included in the analysis. Fifty-eight patients (50%) were male, and the median age at baseline was 28 years. At W24, 87 patients (74%; 95% confidence interval [CI], 65.5%–82.0%; n = 117) achieved ADA success. Among the 30 patients with ADA failure, 15 underwent surgery. At W104, the survival rate without abscess recurrence or surgery was 72.9% (95% CI, 62.1%–79.8%; n = 109). Abscess drainage was significantly associated with ADA failure at W24 (odds ratio, 4.18; 95% CI, 1.06–16.5; *P* =0 .043). Disease duration (hazard ratio [HR], 1.32; 95% CI, 1.09–1.59; *P* = .008), abscess drainage (HR, 5.59; 95% CI, 2.21–14.15; *P* = .001), and inflammatory changes in mesenteric fat (HR, 0.4; 95% CI, 0.17–0.94; *P* = .046) were significantly associated with ADA failure at W104.**

CONCLUSION: **Provided that the abscess was carefully managed before initiating medical treatment, this study showed the high efficacy of ADA in the short and long term in biologic-naïve patients with CD complicated by an intra-abdominal abscess. ClinicalTrials.gov, Number: NCT02856763**

Keywords: Abscess; Adalimumab; Anti-TNF; Crohn's Disease; Surgery.

Crohn's disease (CD) is a chronic inflammatory bowel disease (IBD) that generally evolves through acute flare-ups with periods, of remission, ultimately leading to the appearance of intestinal complications such as perforation, bowel obstruction, or intra-abdominal abscesses.[1,2] Abdominal or pelvic abscesses complicate the clinical course of CD in 10% to 30% of patients.[3-5] Moreover, 15% of patients with an inflammatory or stricturing phenotype of the disease will progress toward a penetrating phenotype during the first 5 years of the follow-up.[6]

The first phase of intra-abdominal abscess management is now well-standardized and includes sepsis resolution with the use of systemic antibiotics and drainage of the infected fluid collection, when feasible.[7] Over the past 2 decades, radiologic-guided percutaneous drainage has been increasingly used, especially when the abscess is easily accessible, well-defined, and unilocular.[8] Despite the clear consensus on how to early treat sepsis and abscesses, the overall management of CD complicated by an intra-abdominal abscess remains challenging. After initial treatments allowing optimizing the general condition of the patient and ensuring a relatively sterile operating field, most experts recommend performing a delayed resection of the perforated intestinal segment, especially in case of obstructive symptoms.[7] Indeed, it is widely acknowledged that patients with CD developing intestinal perforations have an advanced-stage disease that fails to respond to medical treatment.[9]

The use of anti-TNF antibodies has improved the success of medical therapy in CD patients with an intra-abdominal abscess as they have been shown to alter the natural course of CD by inducing mucosal healing and reducing hospitalization and surgery rates.[10,11] Only 2 retrospective monocenter studies have assessed the use of infliximab or adalimumab in CD complicated by an intra-abdominal abscess with encouraging results.[12,13] There are no data available in the literature on the use of other biologics in biologic-naïve patients with CD complicated by an intra-abdominal abscess. Therefore, the aims of this prospective study were to assess the success rate and safety of adalimumab in biologic-naïve patients with CD complicated by an intra-abdominal abscess after complete resolution of sepsis and abscess and to identify predictive factors for success of this medical strategy.

Materials and Methods

Study Design and Patients

Investigators from the Groupe d'Etudes Thérapeutiques des Affections Inflammatoires du Tube Digestif

(GETAID) designed this prospective, multicenter, open-label, observational study. This study was registered with the MICA ClinicalTrials.gov number NCT02856763. All consecutive patients with luminal CD complicated by an intra-abdominal or pelvic abscess consulting in one of the participating GETAID centers were identified and screened for the study. To be included, patients had to be at least 18 years and to meet the following inclusion criteria: (1) a diagnosis of CD (confirmed by a clinical evaluation and a combination of endoscopic, histological, radiological, and/or biochemical investigations according to European guidelines,[14] (2) a diagnosis of spontaneous intra-abdominal or pelvic abscess according to radiological criteria confirmed by ultrasound, computed tomography (CT) scan or magnetic resonance enterography (MRE); and (3) an inadequate response or intolerance to corticosteroids and/or immunosuppressants, or a medical contraindication to such therapies. Patients with a postoperative abscess (occurring within 12 weeks of intestinal resection), a need for immediate surgery due to irreversible intestinal obstruction, peritonitis or uncontrolled sepsis, a perineal abscess, an isolated intra-parietal abscess in the small intestine or colon, an abscess occurring under anti-TNF therapy, a previous failure or intolerance to adalimumab, pregnancy or breastfeeding, contraindications to MRE, and with a contraindication to anti-TNF treatment were excluded.

The study protocol was approved by the Institutional Review Board, CPP Ile de France IV (IRB number 00003835). All patients gave their written consent to participate in the study.

Procedures

Before inclusion in the study and adalimumab initiation, all patients received a prespecified management of the intra-abdominal abscess according to European guidelines,[7] consisting of systemic antibiotics and radiologic-guided percutaneous abscess drainage, when feasible. When percutaneous drainage was not possible, antibiotics alone were continued in case of small abscess (<30 mm in diameter). The abscess features are detailed in Supplementary Table 1. In the absence of improvement after antibiotic treatment, surgical drainage was considered for larger abscesses. A minimum duration of systemic antibiotics of 2 weeks was recommended in case of drainage and 3 weeks when drainage was not feasible. Infliximab and adalimumab are the anti-TNF treatment options currently available for patients with CD. Adalimumab was chosen as study treatment in this patient cohort because of its greater ease of use and to have a more homogeneous cohort in terms of treatment. Adalimumab was initiated just after antibiotic discontinuation in case of drainage. Maintenance or discontinuation of immunosuppressants in previously treated patients was at the referring physician's discretion. Steroid tapering during abscess management was recommended. The MRE examination is described in Supplementary Appendix 2.

What You Need to Know

Background

Management of intra-abdominal abscess complicating Crohn's disease is challenging. Surgery with delayed intestinal resection is usually recommended after abscess resolution. Some retrospective data suggest that anti-TNF therapy may be effective in this situation and avoid surgery.

Findings

Once the intra-abdominal abscess has been successfully controlled, medical treatment with adalimumab avoids the need for surgery in up to three-quarters of patients with 2 years of follow-up. Drainage of the abscess is associated with a lower effectiveness of the adalimumab treatment.

Implications for patient care

Intestinal resection surgery after complete resolution of an intra-abdominal abscess should no longer be considered as first-line treatment but only after considering the possibility of disease-modifying anti-TNF therapy.

Patients showing a complete resolution of the abscess on baseline MRE and a resolution of sepsis were included in the study and received a first subcutaneous injection of adalimumab at a dose of 160 mg at baseline (week [W] 0), followed by 80 mg at W2, and then 40 mg every other week as shown in Supplementary Figure 1. The first dose of adalimumab had to be administered less than 21 days after MRE performed to confirm abscess resolution. Adalimumab dosage (dose, frequency of administration) was then left at the physician's discretion. Small bowel stricture was defined as a localized luminal narrowing (diameter reduction by at least 50%), with bowel wall thickening (increase >25% compared with the adjacent non-affected bowel), and pre-stricture dilation (>30 mm).[15]

Patients were assessed using the Crohn's Disease Activity Index (CDAI), complete blood cell count, and C-reactive protein (CRP) serum level within 3 weeks before baseline and at W8, W16, and W24 or at the time of study withdrawal. Obstructive symptoms during the last 8 weeks were assessed using the Crohn's Disease Obstructive Score (CDOS)[16] at W0, W8, W16, and W24. Patients were followed from W24 to W104. In the event of study discontinuation, failure/intolerance to adalimumab, or surgical resection/abscess recurrence was recorded for all withdrawn patients.

Outcome Measures

The primary endpoint was adalimumab success at W24 defined as the absence of steroid use after W12, abscess recurrence, intestinal resection, clinical relapse

(CDAI >220 or Harvey-Bradshaw Index >4) and a CRP level >10 mg/L on 2 consecutive visits), while adalimumab treatment was continued. The secondary post-hoc endpoint was the long-term success of adalimumab defined as patients' survival in the absence of abscess recurrence or surgery within the first 104 weeks. The association between the baseline factors and adalimumab failure was investigated to identify predictive factors for the short- (W24) and long-term (W104) outcomes of adalimumab treatment.

To assess adalimumab safety, any significant adverse event (AE) reported by the patients who received at least 1 injection of adalimumab between baseline and the last follow-up visit, was recorded. Serious adverse events (SAEs) were defined as any fatal or life-threatening event resulting in one of the following situations: hospitalization, extension of a hospital stay, or disability.

Statistical Analysis

Descriptive statistics were used to describe the baseline characteristics of the study population and all AEs reported throughout the follow-up. The median and interquartile range (IQR) were calculated for continuous data and counts, and percentages were computed for discrete data. Survival in the absence of abscess recurrence and surgery at W104 was analyzed using the Kaplan-Meier test.

Univariate analyses were performed to assess the rates of short- (W24) and long-term (before W104) failure, using respectively a logistic model and a Cox proportional hazards model, to take into account the failure rate and the differences in follow-up. All covariates from the univariate analyses with less than 25% of missing values were considered as candidate predictors to be included in a multivariable model. Multiple imputation was performed to replace missing data with m imputations.[17] A stepwise Akaike information criterion forward method for variable selection was used for each of the m imputed datasets. The final model was constructed using the covariates that were the most frequently selected in the m models. The final coefficients were estimated by running the final model for each of the m imputed datasets, and pooling coefficients using Rubin's rules.[18,19]

Additionally, for both short- and long-term outcomes, a post-hoc subgroup analysis was performed in patients whose abscess was not drained during the initial management.

Results

From April 2013 to December 2017, 190 patients with CD with an intra-abdominal abscess were screened in 27 GETAID centers. All tests and procedures performed from patients' screening to the end of the follow-up are described in Supplementary Figure 2.

Patients' Baseline Characteristics

The main baseline characteristics of the studied cohort are presented in Table 1. Disease activity at baseline was assessed using the CDAI or Harvey-Bradshaw Index. CD was considered quiescent in 66 patients (63%) and active in 38 patients (37%).

Abscess Features and Management

Patients received systemic antibiotics during the first phase of abscess management for a median time of 22 days (IQR, 8–31 days). In addition to antibiotic treatment, the abscess was drained in 11 patients (9%). Among them, 8 (73%) underwent a radiologic-guided percutaneous drainage and 3 (27%) underwent a surgical drainage. The median duration of abscess drainage was 13 days (IQR, 7–28 days), and it was successful in 3 patients. In the remaining patients, the radiologic-guided percutaneous drainage had to be repeated and was successful. The abscess was not drained in 106 patients due to the small size of the abscess in 59 patients (67%) and to the difficulty of accessing the abscess site in 29 patients (33%) (the reason was available for only 88 patients). Table 2 shows the abscess features and management implemented for the 117 patients with CD with an intra-abdominal abscess included in the analysis.

All patients underwent MRE just before adalimumab initiation to assess intra-abdominal abscess resolution and to allow an accurate description of the intestinal lesion. The parameters recorded during MRE are presented in Table 3. In particular, internal fistula and intestinal stricture were still present in 40 (35%) and 9 (8%) patients, respectively.

Success of Adalimumab Therapy

At W24, adalimumab therapy was successful in 87 of the 117 (74%; 95% confidence interval [CI], 65.5–82.0) patients and failed in 30 patients. Treatment failure was due to a clinical relapse in 7 patients, for which corticosteroids were needed in 4 patients, a recurrence of the intra-abdominal abscess in 15 patients, and an intestinal resection in 15 patients. The main indications for surgical treatment were stenosis (n = 5) or recurrence of the abscess (n = 8). In the other situations, it was indicated for an occlusion and a fistula (n = 2).

Eight patients early discontinued the study before W104 and were not included in the W104 analysis. At W104, treatment failure was observed in 31 of the 109 patients (28.4%). Among these 31 cases of treatment failure, the intestinal abscess relapsed with no need for surgery in 4 patients, and the remaining 27 patients underwent surgical resection, which was due to abscess recurrence in 13 cases. The reasons for adalimumab failure at W24 and W104 are presented in Supplementary Table 2. Over the 2-year study period, 49

Table 1. Baseline Characteristics

Variables	Value
Gender, n (%)	
Male	58 (49.6)
Female	59 (50.4)
Age at baseline (n = 117), *y*	27.98 (23.66–35.78)
Duration of disease prior to the diagnosis of the abscess (n = 114), *months*	2.348 (0–58.65)
Smoking	
Never/history	72 (64.9)
Active	39 (35.1)
Missing	6
Harvey-Bradshaw Index at baseline (n = 86)	3 (2–5)
CDAI at baseline (n = 89)	97.7 (51.4–135.9)
Activity at baseline	
Quiescent	66 (63)
Active	38 (37)
Obstructive symptoms at baseline	
No or mild symptoms	52 (71)
Moderate or severe symptoms	21 (29)
Missing	44
Treatments at baseline (n = 117)	
Ongoing budesonide	13 (11)
Ongoing systemic steroids	27 (23)
Prior treatment with thiopurines	33 (28)
Ongoing immunosuppressants	34 (29)
Nutrition at baseline	
None or other nutrition support	45 (38.5)
Exclusive enteral or parenteral food	72 (61.5)
Height, *cm*	170 (165–179)
Weight index (n = 104), *kg*	65 (57–75)
Weight at baseline (n = 117), *kg*	61 (54–70)
BMI (n = 117), kg/cm^2	20.8 (18.9–22.8)
Albuminemia (n = 80), *g/L*	39 (36–43)
Inflammatory markers at baseline (n = 117)	
Leukocytes(n = 106), $10^9/L$	6.9 (5.7–8.9)
CRP (n = 104), *mg/L*	5 (2–9)

Note: Data are presented as number (%) or median (interquartile range).
BMI, Body mass index; CDAI, Crohn's disease activity index; CRP, C-reactive protein.

of the 117 (37.2%; 95% CI, 28.1%–46.3%) patients discontinued adalimumab treatment due to drug intolerance, a loss of response or for other reasons in 6, 36, and 11 cases, respectively.

The rate of adalimumab failure did not significantly differ between patients treated or not with immunosuppressants as shown in Supplementary Table 3. The Kaplan-Meier curve (Figure 1) shows the probability of survival in the absence of abscess relapse or surgery over the 2-year follow-up. The 1- and 2-year survival probabilities were 77.5% (95% CI, 70.2%–85.5%) and 72.9% (95% CI, 62.1%–79.8%; n = 109), respectively. The survival probability in the absence of intestinal resection was 75.4% (95% CI, 67.7%–84.0%) at W104.

Factors Associated With Adalimumab Success at W24

Table 4 shows the results of the univariate and pooled multivariate analyses at W24. In the multivariate model, only 1 of the 4 covariates analyzed was significantly associated with treatment failure: abscess drainage at baseline (odds ratio [OR], 4.18; 95% CI, 1.06–16.5; $P = .043$), high mural signal intensity on T2-weighted MRE (OR, 0.44; 95% CI, 0.16–1.16; $P = .1$), a family history of IBD (OR, 2.49; 95% CI, 0.85–7.3; $P = .098$), and the smoking status (OR, 2.38; 95% CI, 0.96–5.9; $P = .064$). However, in the subgroup analysis in non-drained patients, the "high mural signal intensity on T2-weighted MRE" covariate reached significance (OR, 0.30; 0.11–0.82; $P = .021$).

Factors Associated With Adalimumab Success at W104

Table 5 shows the results of the univariate and pooled multivariate analyses at W104. In the multivariate model, the following 3 covariates were significantly associated with treatment failure: disease duration before abscess occurrence (hazard ratio [HR], 1.32; 95% CI, 1.09–1.59; $P = .008$), abscess drainage (HR, 5.59; 95% CI, 2.21–14.15; $P = .001$), and inflammatory changes in mesenteric fat (HR, 0.4; 95% CI, 0.17–0.94; $P = .046$). In the subgroup analysis, only the "disease duration before abscess occurrence" covariate remained significant (HR, 1.36; 95% CI, 1.13–1.6; $P = .004$), and the other 2 covariates were no longer significant.

Safety

Among patients who received at least 1 dose of adalimumab, 128 were included in the safety analysis. A total of 290 AEs were observed in 96 patients exposed to adalimumab so that a median number of 3 AEs (IQR, 1–4 AEs) per patient was reported among patients experiencing at least 1 AE. Of the 290 AEs, 73 (25%) were deemed serious and experienced by 45 patients (15.5%) exposed to adalimumab. Forty-eight SAEs were classified as "gastrointestinal disorders" and were experienced by 31 patients, 21 SAEs were classified as "infections and infestations" and were experienced by 17 patients. Thirty-two patients treated with adalimumab did not experience any AEs. These 290 AEs are detailed in Supplementary Table 4.

None of the patients required intensive care unit admission during the follow-up, and 1 death event was reported among the screened patients who did not receive adalimumab.

Table 2. Abscess Features and Early Management

Variables	Value
Type of imaging for the diagnosis of the abscess	
Ultrasound	6 (5)
CT scan	91 (78)
MRE	19 (16)
Missing	1
Number of abscesses	
1	95 (81)
2	20 (17)
>2	2 (2)
Diameter of the largest abscess (n = 110), *mm*	29 (20–45)
Location of CD leading to the abscess	
Small bowel	101 (86)
Colon	16 (14)
Abscess extent	
Lower right abdominal region	37 (45)
Pelvic region	30 (37)
Periumbilical region	6 (7)
Epigastric region	2 (3)
Lower left abdominal region	2 (3)
Multiple extension	5 (6)
Missing	35
Visible draining fistula	
Yes	58 (54)
No	50 (46)
Body temperature at the time of diagnosis of the abscess (n = 85), °C	37.2 (36.9–38.2)
Drainage of the abscess	
Yes	11 (9)
No	106 (91)
Reason for not draining	
Difficulties of accessing the abscess	29 (33)
Insufficient size of the abscess	59 (67)
Missing	18
Type of drainage	
Radiologic-guided percutaneous	8 (73)
Surgical	3 (27)
Drainage duration, *days*	13 (7–29)
Need for a second drainage	
Yes[a]	1 (9)
No	10 (91)
Antibiotic treatment	
Yes	114 (97.4)
No	3 (2.6)
Antibiotic duration, *days*	47 (18–66)

Note: Data are presented as number (%) or median (interquartile range).
CD, Crohn's disease; CT, computed tomography; MRE, magnetic resonance enterography.
[a]This specific patient underwent a second radiologic-guided percutaneous drainage for 6 days with good efficacy.

Table 3. MRE Findings

Variables	Value
Abscess resolution	
Yes	117 (100)
No	0 (0)
Length of small bowel disease (n = 112), cm	15 (10–25)
Mural thickness (n = 114), mm	8 (6.25–10)
High mural signal intensity on T2-weighted MRE[a]	
Yes	85 (75)
No	29 (25)
Missing	3
Mural enhancement intensity in parenchymatous phase[a]	
Marked	65 (56)
Mild to moderate	50 (43)
Absent	1 (1)
Missing	1
Mural enhancement pattern in parenchymatous phase	
Homogenous	40 (35)
Layered	60 (52)
Mixed	15 (13)
Missing	2
Mural enhancement intensity in delayed phase[a]	
Marked	40 (43)
Mild to moderate	46 (50)
Absent	6 (7)
Missing	25
Mural enhancement pattern in delayed phase	
Homogenous	44 (51)
Layered	31 (36)
Mixed	11 (13)
Missing	31
Inflammatory changes in mesenteric fat	
Absent	28 (24)
Blurred wall	47 (41)
Mass or phlegmon without abscess	40 (35)
Missing	2
Fistula (T2 hypersignal in fat, other organ or skin)	
Absent	48 (42)
Blind	26 (23)
Internal	40 (35)
Cutaneous	1 (1)
Missing	2

Note: Data are presented as number (%) or median (interquartile range).
MRE, Magnetic resonance enterography.
[a]Mandatory sequences were breath-hold imaging performed in the coronal plane using a T2-weighted single-shot turbo spin echo sequence and a true fast imaging with balanced steady-state sequence and (after intravenous administration of an antispasmodic agent) a T1-weighted sequence before, 90 seconds and 8 minutes after an intravenous injection of gadolinium chelates. Ninety seconds was the parenchymatous time, and 8 minutes was the delayed enhancement time.

Discussion

The occurrence of an intra-abdominal abscess complicating CD is a relatively common situation that most gastroenterologists may encounter.[6] Although the initial strategy for the management of the abscess is well-codified, the choice of treatment between surgery and medical therapy remains largely empirical. Thus, although surgery with delayed bowel resection remains

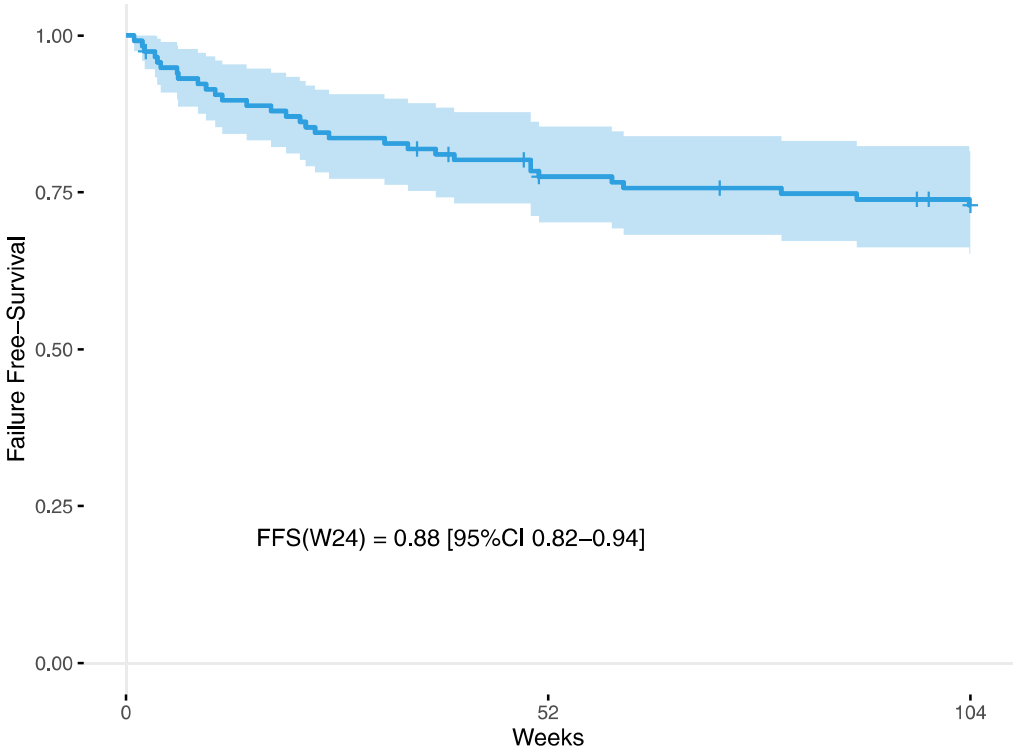

Figure 1. Probability of survival in the absence of abscess relapse or surgery over the 2-year follow-up in 117 patients with Crohn's disease treated with adalimumab after resolution of an intra-abdominal abscess. FFS, Failure-free survival.

the standard treatment in this situation,[7] it is less and less used, suggesting an increasing emphasis on the medical management.[20] Several retrospective studies support the use of medical strategies to avoid surgery and bowel damage in these patients, especially since the introduction of anti-TNFs.[12,13,21] However, further studies are needed to confirm the efficacy and safety of anti-TNFs for the treatment of CD complicated by an intra-abdominal abscess.

In our study, we particularly focused on the quality of abscess management prior to adalimumab initiation, in accordance with European guidelines.[7] Prior to inclusion, patients received systemic antibiotics for at least 2 to 3 weeks to treat sepsis. Percutaneous drainage under radiological guidance was performed whenever indicated and feasible, depending on the abscess size and accessibility. In fact, the abscess of only 9% of patients was drained. This relatively low rate could be explained by the small size of the abscesses, with a mean maximum diameter of 29 mm.

Using a stringent composite endpoint, we showed that adalimumab therapy was successful in 74% of patients during the first 24 weeks. Moreover, 87% of patients did not require intestinal resection, and one-third of the patients who underwent surgery experienced a recurrence of the abscess that did not respond to medical therapy until W24. After a 2-year follow-up, 72.9% of patients with CD with an intra-abdominal abscess did not experience any abscess recurrence and had not undergone intestinal surgery. This was the first study to provide prospective data on the management of patients with CD with an intra-abdominal abscess treated with an anti-TNF.

We used a stepwise logistic regression and a Cox proportional hazards model with multiple imputation to identify factors associated with the short- and long-term success of adalimumab treatment, respectively. Abscess drainage was significantly and positively associated with treatment failure at W24 and W104. At W104, the disease duration before abscess recurrence was positively associated, whereas inflammatory changes in mesenteric fat were negatively associated. Previous monocenter studies have suggested that the intra-abdominal abscess would be more likely to recur in patients with CD with a visible fistula treated with steroids.[21] In our cohort, some of the patients received steroids at baseline, and 54% of included patients had a visible draining fistula due to the abscess. However, our results did not suggest that patients with 1 of these 2 factors were at higher risk of abscess recurrence on adalimumab treatment. A retrospective monocenter study using an adjusted multivariable model has concluded that the bowel wall thickness, the disease duration, bowel dilation, and an abscess size greater than 6 cm were independent risk factors for future surgery in patients not undergoing immediate bowel resection for abscess management.[22] In our study, the abscess size was not identified as a predictive factor because all patients with a persistent abscess after the first management phase were not included. Indeed, persistent intra-abdominal sepsis would not allow initiating biologic treatment because a prolonged antibiotic use and abscess drainage failure are clear indications for intestinal resection. In our cohort, only 9 patients had a significant stricture associated with the intra-abdominal abscess at baseline, and no association was found

Table 4. Factors Associated With Adalimumab Failure at Week 24

	Univariate analysis		Multivariate analysis	
Variables	OR (95% CI)	*P*–value	OR (95% CI)	*P*-value
Gender				
Male	1			
Female	0.68 (0.30–1.57)	.37		
Smoking status				
Never/history	1			
CD activity at baseline	2.13 (0.89–5.06)	.088	2.38 (0.96-5.9)	.064
BMI	0.90 (0.79–1.02)	.11		
Age at diagnosis, *y*	0.97 (0.92–1.01)	.16		
Disease duration before abscess occurrence (<5 years)	1.16 (0.90–1.49)	.26		
Disease duration before abscess occurrence ≥2 years				
No	1			
Yes	1.18 (0.48–2.88)	.72		
Previous surgery for Crohn's Disease				
No	1			
Yes	1.76 (0.48–6.49)	.40		
Family history of inflammatory bowel disease				
No	1			
Yes	1.62 (0.61–4.35)	.33	2.49 (0.85-7.3)	.098
Nutrition at baseline (2 classes)				
None or other nutrition support	1			
Exclusive enteral or parenteral food[a]	1.35 (0.56–3.22)	.50		
Previously exposed to thiopurines				
No	1			
Yes	1.39 (0.57–3.41)	.47		
Budesonide at baseline				
No	1			
Yes	1.33 (0.38–4.69)	.65		
Systemic corticosteroids at baseline				
No	1			
Yes	0.79 (0.28–2.18)	.64		
Hematocrit at baseline	0.92 (0.82–1.03)	.14		
CRP at baseline	1.02 (1.00–1.04)	.13		
Albuminemia at baseline	0.98 (0.88–1.08)	.64		
Leukocytes at baseline	1.05 (0.88–1.26)	.55		
Visible fistula at the time of diagnosis of the abscess				
No	1			
Yes	1.24 (0.51–3.01)	.64		
At least one abscess in the ileum				
No	1			
Yes	2.68 (0.57–12.6)	.21		
At least one abscess in the colon				
No	1			
Yes	0.55 (0.11–2.67)	.46		
Size of the largest abscess	1.01 (0.99–1.03)	.26		

Table 4. Continued

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*P*–value	OR (95% CI)	*P*-value
Location of the largest abscess				
Other	1			
Ileum only	1.67 (0.34–8.25)	.53		
Abscess drainage				
No	1			
Yes	4.10 (1.15–14.6)	.03	4.18 (1.06-16.5)	.043
Stenosis				
Absent	1			
Present	0.71 (0.25–2.03)	.52		
Non-interpretable	0.45 (0.12–1.72)	.24		
Length of small bowel disease[b]	1.01 (0.99–1.03)	.37		
Mural thickness	1.05 (0.89–1.24)	.54		
High mural signal intensity on T2-weighted MRE				
Absent	1			
Present	0.44 (0.18–1.10)	.08	0.44 (0.16;1.16)	.10
In parenchymatous phase: mural enhancement intensity[b]				
Mild or moderate or absent	1			
Marked	1.15 (0.49–2.70)	.75		
In parenchymatous phase: mural enhancement pattern[b]				
Homogeneous	1			
Layered/mixed	1.45 (0.57–3.68)	.43		
In delayed phase: mural enhancement intensity[b]				
Mild to moderate or Absent	1			
Present	0.60 (0.23–1.53)	.28		
In delayed phase: mural enhancement pattern[b]				
Homogeneous	1			
Layered/mixed	3.59 (1.30–9.93)	.014		
Measurement of luminal diameter in the segment proximal to the narrowing	0.99 (0.95–1.04)	.80		
Measurement of luminal diameter in a normal loop	1.04 (0.97–1.11)	.26		
Percentage of narrowing	1.00 (0.98–1.01)	.59		
Inflammatory changes in mesenteric fat[b]				
Absent	1			
Present	0.54 (0.21–1.35)	.19		
Fistula (T2 hypersignal in fat, other organ, or skin)				
Absent	1			
Present	0.92 (0.39–2.12)	.84		
Fibrofatty proliferation				
Absent	1			
Present	0.98 (0.42–2.28)	.96		
Mesenteric lymph node(s) (>3 mm)				
Absent	1			
Present	0.61 (0.26–1.42)	.25		
Size of the lymph nodes	0.84 (0.62–1.14)	.25		

Table 4. Continued

	Univariate analysis		Multivariate analysis	
Variables	OR (95% CI)	*P*–value	OR (95% CI)	*P*-value
Lymph nodes enhancement				
No	1			
Yes	0.38 (0.07–1.90)	.24		
Ganglion inflammation[b]				
No	1			
Yes	0.57 (0.24–1.32)	.19		
Percentage of dilation of the proximal segment lumen compared with the lumen of a normal loop >30%				
No	1			
Yes	0.74 (0.30–1.83)	.51		
Percentage of dilation of the proximal segment lumen compared with the lumen of a normal loop >40%				
No	1			
Yes	0.74 (0.28–1.96)	.54		
Percentage of dilation of the proximal segment lumen compared with the lumen of a normal loop >50%				
No	1			
Yes	0.59 (0.18–1.93)	.39		
Concomitant immunosuppressors				
No	1			
Yes	0.68 (0.26–1.77)	.42		

BMI, Body mass index; CD, Crohn's disease; CI, confidence interval; CRP, C-reactive protein; MRE, magnetic resonance enterography; OR, odds ratio.
[a]These covariates correspond to nutritional support received before adalimumab initiation during the early management phase.
[b]These covariates were determined on control MRE performed just before adalimumab initiation.

between the intestinal stricture and the failure of adalimumab. Indeed, the diagnosis of small bowel stricture based on cross-sectional imaging is challenging due to the existence of various definitions of luminal narrowing, bowel thickness, and upstream luminal dilation. In our study, we used a consensual and unquestionable radiological definition of a small bowel stricture, which could have resulted in an underestimation of the cases of moderate but symptomatic intestinal stricture. It should be noted that, based on the CDOS, most of the included patients had no obstructive symptoms but rather mild-to-moderate symptoms, whereas only 8% had severe obstructive symptoms. Drainage of the abscess was an independent factor for failure at W24, with an OR of 4.18 (95% CI, 1.06–16.5), meaning that the failure rate was higher with drainage. Thus, among the 82 of 106 patients who were not drained, a success rate of 77% was observed, whereas it was only of 45% in the 5 of 11 drained patients. However, the groups were not balanced in terms of numbers, so no reliable comparison could be performed.

A crucial aspect was to assess adalimumab safety in patients with CD with an intra-abdominal abscess. A complete resolution of sepsis and abscess had to be confirmed before anti-TNF initiation. In our study, the risk of life-threatening infection or mortality was low.

The main strength of this study is its prospective and multicenter design. Also, patients with CD with an intra-abdominal abscess were included from 27 hospital facilities all over the French territory. We implemented a pre-management plan for patients with CD with an abscess that allowed carefully preparing them to receive a medical intervention. This could explain the good results observed with the initiation of adalimumab. Nevertheless, we used a very stringent composite endpoint that is clinically relevant when physicians have to manage patients with CD with an intra-abdominal abscess. The good results could also be explained by the early management of the patients, given that all patients were naïve to biologic therapy and the short time between their diagnosis of CD and the occurrence of their abscess. However, this study also has some limitations, including the absence of randomization and the fact that no control group was used. However, it would have been unethical to randomly assign these patients to interventional and placebo groups as they presented with a severe form of the disease with a high risk of severe infectious complications.[13,21] This study was not directed against surgical interventions but recommends its appropriate use for the most suitable patients, in whom the

Table 5. Factors Associated With Adalimumab Failure at Week 104

	Univariate analysis		Multivariate analysis	
Variables	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Gender				
Male	1.00			
Female	1.16 (0.57–2.36)	.68		
Smoking status				
Never/history	1.00			
Active	1.19 (0.58–2.46)	.63		
BMI	0.89 (0.79–1.00)	.055		
Age at diagnosis	0.99 (0.95–1.03)	.54		
Disease duration before abscess occurrence (<5 years)	1.28 (1.08–1.52)	.004	1.32 (1.09; 1.59)	.008
Disease duration before abscess occurrence ≥2 years				
No	1.00			
Yes	2.01 (0.96–4.17)	.062		
CD activity at baseline				
Quiescent	1.00			
Active	1.79 (0.86–3.71)	.12		
Previous surgery for Crohn's disease				
No	1.00			
Yes	2.33 (0.89–6.06)	.084		
Family history of inflammatory bowel disease				
No	1.00			
Yes	1.19 (0.51–2.78)	.68		
Nutrition at baseline (2 classes)				
None or other nutrition support	1.00			
Exclusive enteral or parenteral food [a]	1.16 (0.55–2.42)	.70		
Previously exposed to thiopurines				
No	1.00			
Yes	1.29 (0.61–2.75)	.50		
Budesonide at baseline				
No	1.00			
Yes	1.04 (0.36–2.97)	.94		
Systemic corticosteroids at baseline				
No	1.00			
Yes	1.2 (0.54–2.68)	.66		
Hematocrit at baseline	0.9 (0.82–0.99)	.030		
CRP at baseline	1.01 (1.00–1.02)	.003		
Albuminemia at baseline	0.92 (0.86–1.00)	.037		
Leukocytes at baseline	1.15 (0.99–1.34)	.064		
Visible fistula at the time of diagnosis of the abscess				
No	1.00			
Yes	1.36 (0.63–2.93)	.43		
At least one abscess in the ileum				
No	1.00			
Yes	1.56 (0.47–5.13)	.46		
At least one abscess in the colon				
No	1.00			
Yes	0.83 (0.25–2.74)	.76		
Size of the largest abscess	1.01 (1.00–1.00.02)	.024		
Location of the largest abscess				
Other	1.00			
Ileum only	1.73 (0.41–7.26)	.46		

Table 5. Continued

Variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Abscess drainage				
No	1.00			
Yes	4.08 (1.75–9.48)	.001	5.59 (2.21; 14.15)	.001
Stenosis				
Absent	1.00			
Present	1.05 (0.42–2.59)	.92		
Non-interpretable	0.50 (0.14–1.76)	.28		
Length of small bowel disease[b]	1.00 (1.00–1.01)	.064		
Mural thickness	0.97 (0.84–1.12)	.68		
High mural signal intensity on T2-weighted MRE				
Absent	1.00			
Present	0.49 (0.24–1.02)	.057		
In parenchymatous phase: mural enhancement intensity[b]				
Mild to moderate or absent	1.00			
Marked	0.94 (0.46–1.91)	.87		
In parenchymatous phase: mural enhancement pattern[b]				
Homogeneous	1.00			
Layered/mixed	1.08 (0.51–2.32)	.84		
In delayed phase: mural enhancement intensity[b]				
Mild to moderate or absent	1.00			
Present	0.65 (0.29–1.46)	.29		
In delayed phase: mural enhancement pattern[b]				
Homogeneous	1.00			
Layered/mixed	3.12 (1.29–7.54)	.011		
Measurement of the luminal diameter in the segment proximal to narrowing	0.99 (0.95–1.03)	.55		
Measurement of the luminal diameter in a normal loop	1.05 (1.00–1.09)	.035		
Percentage of narrowing	1.00 (0.99–1.01)	.95		
Inflammatory changes in mesenteric fat[b]				
Absent	1.00			
Present	0.56 (0.26–1.18)	.13	0.4 (0.17; 0.94)	.046
Fistula (T2 hypersignal in fat, other organ, or skin)				
Absent	1.00			
Present	0.86 (0.42–1.74)	.67		
Fibrofatty proliferation				
Absent	1.00			
Present	1.14 (0.56–2.36)	.71		
Mesenteric lymph node(s) (>3 mm)				
Absent	1.00			
Present	0.57 (0.28–1.16)	.12		
Size of the lymph nodes	1.01 (0.79–1.28)	.95		
Lymph node enhancement				
No	1.00			
Yes	0.39 (0.11–1.37)	.14		
Ganglion inflammation[b]				
No	1.00			
Yes	0.53 (0.26–1.00.09)	.084		
Percentage of dilation of the proximal segment lumen compared to the lumen of a normal loop >30%				
No	1.00			
Yes	0.67 (0.30–1.47)	.32		

Table 5. Continued

Variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Percentage of dilation of the proximal segment lumen compared to the lumen of a normal loop >40%				
No	1.00			
Yes	0.66 (0.28–1.55)	.34		
Percentage of dilation of the proximal segment lumen compared to the lumen of a normal loop >50%				
No	1.00			
Yes	0.56 (0.2–1.62)	.29		
Concomitant immunosuppressors				
No	1.00			
Yes	0.55 (0.23–1.35)	.19		

BMI, Body mass index; CD, Crohn's disease; CI, confidence interval; CRP, C-reactive protein; HR, hazard ratio; MRE, magnetic resonance enterography.
[a]These covariates correspond to nutritional support received before adalimumab initiation during the early management phase.
[b]These covariates were determined on control MRE performed just before adalimumab initiation.

administration of an anti-TNF would not be beneficial. Another limitation could be the large number of patients screened and excluded, corresponding to patients in whom medical treatment of the abscess was not successful. This corresponds to a real-life context, and our study provides some elements of response to the 60% of screened patients who were able to receive the study treatment.

In conclusion, this was the first prospective study to assess the effect of adalimumab on the outcomes of patients with CD with an intra-abdominal abscess. Overall, about 72% of patients (79/109) treated with adalimumab benefited from this strategy and did not experience abscess relapse or undergo surgery over the 2-year follow-up. Carefully preparing patients with the administration of antibiotics, percutaneous drainage when feasible, and the assessment of the complete resolution of their abscess is mandatory to choose the most suitable interventional strategy (ie, intestinal resection or anti-TNF treatment).

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.2023.01.013.

References

1. Torres J, Mehandru S, Colombel JF, et al. Crohn's disease. Lancet 2017;389:1741–1755.
2. Cosnes J, Cattan S, Blain A, et al. Long-term evolution of disease behavior of Crohn's disease. Inflamm Bowel Dis 2002; 8:244–250.
3. Keighley MR, Eastwood D, Ambrose NS, et al. Incidence and microbiology of abdominal and pelvic abscess in Crohn's disease. Gastroenterology 1982;83:1271–1275.
4. Nagler SM, Poticha SM. Intraabdominal abscess in regional enteritis. Am J Surg 1979;137:350–354.
5. Steinberg DM, Cooke WT, Alexander-Williams J. Abscess and fistulae in Crohn's disease. Gut 1973;14:865–869.
6. Burisch J, Kiudelis G, Kupcinskas L, et al. Epi-IBD group. Natural disease course of Crohn's disease during the first 5 years after diagnosis in a European population-based inception cohort: an Epi-IBD study. Gut 2019;68:423–433.
7. Adamina M, Bonovas S, Raine T, et al. ECCO Guidelines on therapeutics in Crohn's disease: surgical treatment. J Crohns Colitis 2020;14:155–168.
8. Gervais DA, Hahn PF, O'Neill MJ, et al. Percutaneous abscess drainage in Crohn disease: technical success and short- and long-term outcomes during 14 years. Radiology 2002; 222:645–651.
9. Brihier H, Nion-Larmurier I, Afchain P, et al. Intestinal perforation in Crohn's disease. Factors predictive of surgical resection. Gastroenterol Clin Biol 2005;29:1105–1111.
10. Sandborn WJ. Current directions in IBD therapy: what goals are feasible with biological modifiers? Gastroenterology 2008; 135:1442–1447.
11. Present DH, Rutgeerts P, Targan S, et al. Infliximab for the treatment of fistulas in patients with Crohn's disease. N Engl J Med 1999;340:1398–1405.
12. Cullen G, Vaughn B, Ahmed A, et al. Abdominal phlegmons in Crohn's disease: outcomes following antitumor necrosis factor therapy. Inflamm Bowel Dis 2012;18:691–696.
13. Nguyen DL, Sandborn WJ, Loftus EV Jr, et al. Similar outcomes of surgical and medical treatment of intra-abdominal abscesses in patients with Crohn's disease. Clin Gastroenterol Hepatol 2012;10:400–404.
14. Maaser C, Sturm A, Vavricka SR, et al. European Crohn's and Colitis Organisation [ECCO] and the European Society of Gastrointestinal and Abdominal Radiology [ESGAR]. ECCO-ESGAR Guideline for diagnostic assessment in IBD, part 1: initial diagnosis, monitoring of known IBD, detection of complications. J Crohns Colitis 2019;13:144–164.
15. Rieder F, Bettenworth D, Ma C, et al. An expert consensus to standardise definitions, diagnosis and treatment targets for anti-fibrotic stricture therapies in Crohn's disease. Aliment Pharmacol Ther 2018;48:347–357.
16. Bouhnik Y, Carbonnel F, Laharie D, et al. GETAID CREOLE Study Group. Efficacy of adalimumab in patients with Crohn's

disease and symptomatic small bowel stricture: a multicentre, prospective, observational cohort (CREOLE) study. Gut 2018; 67:53–60.

17. van Buuren S, Brand JPL, Groothuis-Oudshoorn CGM, et al. Fully conditional specification in multivariate imputation. J Statistic Comput Simulat 2016;76:1049–1064.
18. Wood AM, White IR, Royston P. How should variable selection be performed with multiply imputed data? Stat Med 2008; 27:3227–3246.
19. Steyerberg EW, Harrell FE Jr, Borsboom GJ, et al. Internal validation of predictive models: efficiency of some procedures for logistic regression analysis. J Clin Epidemiol 2001;54:774–781.
20. Perera LP, Ananthakrishnan AN, Guilday C, et al. Dyssynergic defecation: a treatable cause of persistent symptoms when inflammatory bowel disease is in remission. Dig Dis Sci 2013; 58:3600–3605.
21. Nguyen DL, Nguyen ET, Bechtold ML. Outcomes of initial medical compared with surgical strategies in the management of intra-abdominal abscesses in patients with Crohn;s disease: a meta-analysis. Eur J Gastroenterol Hepatol 2015;27:235–241.
22. Perl D, Waljee AK, Bishu S, et al. Imaging features associated with failure of nonoperative management of intraabdominal abscesses in Crohn disease. Inflamm Bowel Dis 2019; 25:1939–1944.

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See Supplementary Appendix 1 for the list of investigators of the MICA-GETAID Study Group

Conflicts of interest

These authors disclose the following: Yoram Bouhnik declares fees from Abbvie, Amgen, Biogaran, Biogen, Boehringer Ingelheim, Celltrion, Ferring, Fresenius Kabi, Galapagos, Gilead, Hospira, Janssen, Lilly, Mayoli Spindler, Merck, MSD, Norgine, Pfizer, Roche, Sandoz, Sanofi, Shire, Takeda, and UCB. Guillaume Pineton de Chambrun declares lecture fees from Pfizer, MSD, AbbVie, Takeda and Ferring; and consulting fees from Takeda, Tillots Pharma, and Janssen. Maria Nachury received board membership, consultancy, or lecture fees from Abbvie, Adacyte, Amgen, Arena, Biogen, CTMA, Celltrion, Ferring, Fresenius-Kabi, Janssen, Mayoli-Spindler, MSD, Pfizer, and Takeda. Philippe Seksik reports consulting fees from Pfizer, Astellas, Janssen, Fresenius Kabi, Takeda, Abbvie, Merck-MSD, Pilège, and Biocodex; and grants from Biocodex and Janssen. Romain Altwegg declares lecture fees from MSD, Abbvie, Pfizer, Takeda, and Janssen. Lucine Vuitton received fees from Abbvie, Amgen, MSD, Ferring, Takeda, Pfizer, Celltrion, Janssen, Gilead, Mayoli Spindler, and Mylan. Carmen Stefanescu declares fees from Abbvie, Amgen, Janssen, MSD, Pfizer, Takeda, and Tillots. Stéphane Nancey declares lecture fees from Pfizer, MSD, AbbVie, Takeda, Ferring, Janssen, Lilly, and Novartis; and consulting fees from AbbVie, Takeda, Tillots Pharma, and Janssen. Mélanie Serrero declares boarding or lecture fees from Abbvie, Amgen, Biogen, Celltrion, Ferring, Janssen, Pfizer, MSD, and Takeda. Jerome Filippi declares fees from Abbvie, Amgen, Biogen, Celltrion, Gilead, HAC pharma, Janssen, MSD, Pfizer, Sandoz, Takeda, and Tillotts. Stéphanie Viennot declares lecture fees from Pfizer, MSD, AbbVie, Takeda, and Janssen; and consulting fees from Takeda, and Janssen. Vered Abitbol declares fees from Biogen, Abbvie, Takeda, Janssen, Amgen, Pfizer, Amgen, Vifor, Arkopharma, and UCB. Arnaud Bourreille declares lecture or consulting fees from Abbvie, Amgen, Celltrion, Ferring, Fresenius Kabi, Galapagos, Gilead, Janssen, MSD, OSE Immunotherapeutics, Pfizer, Roche, Takeda, and Tillotts. Cyrielle Gilletta declares lecture fees from Abbvie, Biogen, Fresenius, Janssen, MSD, Pfizer, and Takeda; and consulting fees from Abbvie, Celltrion, and Janssen. Anthony Buisson declares consulting fees for Abbvie, Amgen, Arena, Biogen, Celtrion, CTMA, Galapagos, Janssen, MSD, Nexbiome, Pfizer, Roche, Takeda, and Tillotts; and lecture fees for Abbvie, Amgen, Biogen, Galapagos, Janssen, Mayoli-Spindler, MSD, Norgine, Pfizer, Roche, Takeda, Tillotts, and Vifor Pharma. Xavier Roblin declares consulting fees for Abbvie, Amgen, Biogen, Celtrion, Galapagos, Janssen, MSD, Pfizer, Takeda, and Tillotts; and lecture fees for Abbvie, Amgen, Biogen, Galapagos, Janssen, Ferring, MSD, Pfizer, Takeda, Tillotts, and HAC Pharma. Georgia Malamut declares travel accommodations from Amgen and Janssen. Aurélien Amiot declares consulting fees from Abbvie, Hospira, Takeda, Gilead, and Biocodex; lecture fees and travel accommodations from Abbvie, Janssen, Biocodex, Ferring, Takeda, and MSD; and advisory board fees from Gilead, Takeda, and Abbvie. Mathurin Fumery declares financial support from Abbvie, MSD, Ferring, Boehringer, Pfizer, Takeda, Biogen, Amgen, Gilead, Sandoz, Celgene, Galapagos, Janssen, and Tillots Pharma. Edouard Louis declares research grants from Janssen, Pfizer, Ferring, Falk, Abbvie, and Takeda; educational grants from AbbVie, Janssen, Fresenius-Kabi, and Takeda; speaker fees from Abbvie, Falk, Ferring, Janssen, Pfizer, Galapagos, and Takeda; advisory board fees from Abbvie, Celgene, Ferring, Janssen, BMS, Pfizer, Takeda, Galapagos, Gilead, Arena, and Elli Lilly; and consultant fees from AbbVie. Laurent Peyrin-Biroulet declares fees from Abbvie, Janssen, MSD, Pfizer, Celltrion, Biogen, and Takeda. The remaining authors disclose no conflicts.

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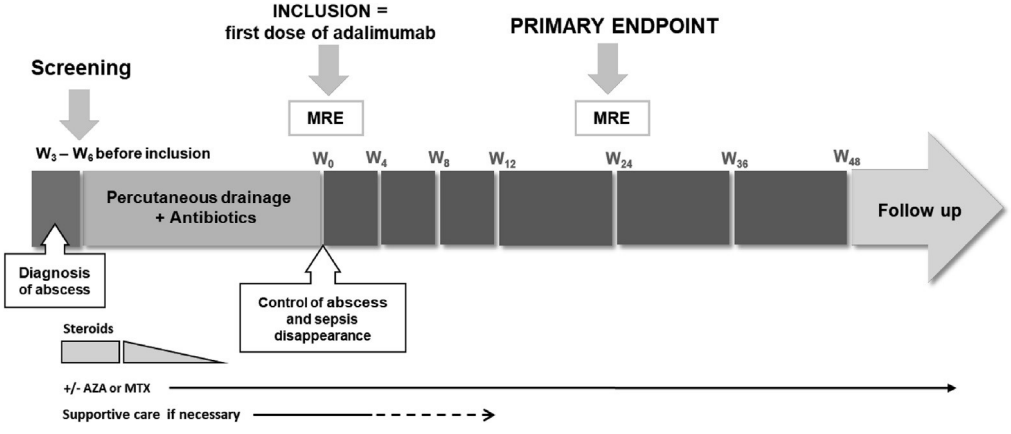
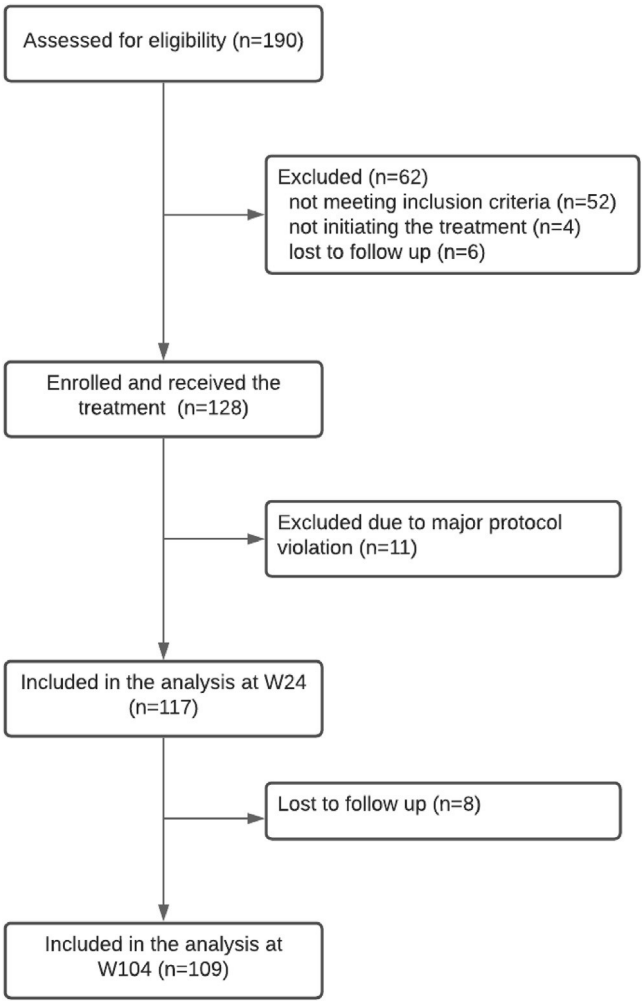
Supplementary Appendix 2. Description of Magnetic Resonance Enterography Examination

Magnetic resonance enterography (MRE) was performed just before baseline in all patients on 1.5 or 3 T systems. All MRE were performed after the oral administration of 1200 mL of hyperosmotic water solution. Mandatory sequences were breath-hold imaging performed in the coronal plane using a T2-weighted single-shot turbo spin echo sequence and a true fast imaging with balanced steady-state sequence. After the intravenous administration of an antispasmodic agent, a T1-weighted sequence 90 seconds before and 8 minutes after the intravenous injection of gadolinium chelates was accomplished. Ninety seconds refers to the parenchymatous time and 8 minutes to the delayed enhancement time.



Supplementary Figure 1. Scheme of the study design.



Supplementary Figure 2. Flow chart describing the recruitment and follow up evaluation of the patients.

Supplementary Table 1. Overall Description of the Abscesses of the Patients Included in the Study

Parameters	Values	N	Statistics
Size of the largest abscess, mm			117
		110	29 (20–44.75)
Location of the largest abscess	Colon	6	5.6%
	Ileum	96	89.7%
	Ileum + colon	5	4.7%
	NA	10	
	Other	11	10.3%
Visible fistula in at least one abscess	No	50	46.3%
	Yes	58	53.7%
	NA	9	
At least one abscess in the duodenum	No	117	100%
At least one abscess in the jejunum	No	117	100%
At least one abscess in the ileum	No	16	13.7%
	Yes	101	86.3%
At least one abscess in the colon	No	105	89.71%
	Yes	12	10.3%
Imaging performed for diagnosis	US	6	5.2%
	CT	91	78.4%
	MRI	19	16.4%
Number of abscesses	NA	1	
	1	95	81.2%
	2	20	17.1%
	3	1	0.9%
	5	1	0.9%
Abscess extent	Epigastric region	2	2.4%
	Lower left	2	2.4%
	Lower right	37	45.1%
	Lower right + upper right	1	1.2%
	Periumbilical region		
	Pelvic region	30	36.6%
	Pelvic region + Lower left	1	1.2%
	Pelvic region + Lower right	1	1.2%
	Periumbilical region	6 7.3%	
	Upper right + Upper left	1 (1.2%) upper right + upper left + 1 (1.2%) periumbilical region	
	NA	35	

CT, Computed tomography; MRI, magnetic resonance imaging; NA, not available ; US, ultrasound.

Supplementary Table 2. Reasons for Adalimumab Failure

Reason for failure	n (%)
Week 24[a]	N = 30
Clinical relapse	1 (3)
Intra-abdominal abscess recurrence[a]	2 (7)
Surgical intersection[b]	2 (7)
Steroids intake + adalimumab interruption	1 (3)
Intra-abdominal abscess recurrence[a] + adalimumab interruption	5 (17)
Steroids intake + clinical relapse + adalimumab interruption	2 (7)
Surgical intersection[b] + adalimumab interruption	4 (13)
Intra-abdominal abscess recurrencea + Surgical intersectionb + adalimumab interruption	7 (23)
Steroids intake + intra-abdominal abscess recurrencea + surgical intersectionb + adalimumab interruption	1 (3)
Other	2 (7)
Adalimumab interruption + other	2 (7)
Surgical intersection[b] + adalimumab interruption + other	1 (3)
Week 104[b]	N = 31
Intra-abdominal abscess recurrence	4 (12.9)
Surgical intersection	14 (45.2)
Intra-abdominal abscess recurrence + surgical intersection	13 (41.9)

[a]The total number of patients who had intra-abdominal abscess recurrence is 15.
[b]The total number of patients who had intestinal resection is 15, and eight patients had a surgical intersection following an intra-abdominal abscess recurrence.

Supplementary Table 3. Treatment Failure Broken Down by Immunosuppressant Treatment

	Concomitant immunosuppressants, n (%)		
Treatment failure	Yes	No	*P*-value
Week 24			
Yes	7 (21)	23 (28)	.49
No	27 (79)	60 (72)	
Week 104			
Yes	6 (19)	25 (32)	.24
No	25 (81)	53 (68)	

Supplementary Table 4. Adverse Events in Patients Exposed to Adalimumab

Type of adverse event	n (%), N = 290
Gastrointestinal disorders	90 (31.0)
Infections and infestations	74 (25.5)
Skin and subcutaneous tissue disorders	33 (11.4)
General disorders and administration site conditions	19 (06.6)
Musculoskeletal and connective tissue disorders	17 (05.9)
General system disorders NEC	09 (03.1)
Metabolism and nutrition disorders	08 (02.8)
Blood lymphatic system disorders	05 (01.7)
Eye disorders	04 (01.4)
Investigations	04 (01.4)
Nervous system disorders	04 (01.4)
Renal and urinary disorders	04 (01.4)
Cardiac disorders	03 (01.0)
Immune system disorders	03 (01.0)
Psychiatric disorders	03 (01.0)
Hepatobiliary disorders	03 (01.0)
Pregnancy puerperium and perinatal conditions	02 (00.7)