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# Shorter Disease Duration Is Associated With Higher Rates of Response to Vedolizumab in Patients With Crohn's Disease But Not Ulcerative Colitis

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**BACKGROUND & AIMS:** Patients with Crohn's disease (CD), but not ulcerative colitis (UC), of shorter duration have higher rates of response to tumor necrosis factor (TNF) antagonists than patients with longer disease duration. Little is known about the association between disease duration and response to other biologic agents. We aimed to evaluate response of patients with CD or UC to vedolizumab, stratified by disease duration.

**METHODS:** We analyzed data from a retrospective, multicenter, consortium of patients with CD (n = 650) or UC (n = 437) treated with vedolizumab from May 2014 through December 2016. Using time to event analyses, we compared rates of clinical remission, corticosteroid-free remission (CSFR), and endoscopic remission between patients with early-stage (≤2 years duration) and later-stage (>2 years) CD or UC. We used Cox proportional hazards models to identify factors associated with outcomes.

**RESULTS:** Within 6 months initiation of treatment with vedolizumab, significantly higher proportions of patients with early-stage CD, vs later-stage CD, achieved clinical remission (38% vs 23%), CSFR (43% vs 14%), and endoscopic remission (29% vs 13%) ( $P < .05$  for all comparisons). After adjusting for disease-related factors including previous exposure to TNF antagonists, patients with early-stage CD were significantly more likely than patients with later-stage CD to achieve clinical remission (adjusted hazard ratio [aHR], 1.59; 95% CI, 1.02–2.49), CSFR (aHR, 3.39; 95% CI, 1.66–6.92), and endoscopic remission (aHR, 1.90; 95% CI, 1.06–3.39). In contrast, disease duration was not a significant predictor of response among patients with UC.

**CONCLUSIONS:** Patients with CD for 2 years or less are significantly more likely to achieve a complete response, CSFR, or endoscopic response to vedolizumab than patients with longer disease duration. Disease duration does not associate with response vedolizumab in patients with UC.

**Keywords:** Inflammatory Bowel Disease; Integrin; Monoclonal Antibody Therapy; Time.

<sup>a</sup>Authors share co-senior authorship.

**Abbreviations used in this paper:** aHR, adjusted hazard ratio; CD, Crohn's disease; CI, confidence interval; CSFR, corticosteroid-free remission; HR, hazard ratio; IBD, inflammatory bowel disease; TNF, tumor necrosis factor; UC, ulcerative colitis.

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Crohn's disease (CD) and ulcerative colitis (UC) are inflammatory bowel diseases (IBD) that result in chronic inflammation of the gastrointestinal tract with periods of remission alternating with relapse.<sup>1,2</sup> It is increasingly recognized that IBD, and CD in particular, are progressive diseases in which patients accumulate bowel damage over time that can lead to irreversible complications.<sup>3-5</sup> There seems to be an optimal window of opportunity in which early effective intervention may improve outcomes and alter the natural history of the disease, akin to the evolving practice in rheumatoid arthritis.<sup>6,7</sup>

Accumulating evidence suggests that treatment with biologics targeting tumor necrosis factor (TNF)- $\alpha$  may be more effective when initiated early in the disease course. In a post hoc analysis of the PRECiSE 2 trial of certolizumab in CD, patients with disease duration less than 2 years had an 82% response rate at 26 weeks, compared with 59% among those with longer disease duration.<sup>8</sup> Similar findings emerged from post hoc analyses of the CHARM trial of adalimumab in CD, where higher clinical remission rates at 56 weeks were seen among patients with disease duration less than 2 years (43%) compared with 2-5 years (30%) or greater than 5 years (28%), even after controlling for potential confounding factors, such as prior TNF antagonist exposure.<sup>9</sup>

Whether this treatment-modifying effect of early disease duration is unique to the TNF antagonist drug class or extends to other treatment agents (eg, anti-integrins) is not clear. A post hoc analysis of the ENCORE trial of natalizumab in CD found that disease duration  $\leq 3$  years was associated with a higher proportion of patients in clinical remission at 12 weeks than the overall treatment population (52% vs 38%).<sup>10</sup> No studies published to date have evaluated response and remission rates to vedolizumab stratified by disease duration.

We aimed to evaluate the impact of disease duration on vedolizumab effectiveness using a multicenter consortium cohort study of the real-world experience with vedolizumab. We analyzed rates of clinical and endoscopic remission in patients with CD and UC treated with vedolizumab, comparing those with shorter disease duration ( $\leq 2$  years) with those with longer-standing ( $> 2$  years) disease.

## Methods

### Study Design

This is a retrospective review of the VICTORY Consortium registry.<sup>11</sup> In brief, this is a multicenter collaborative research group repository where outcomes are pooled for patients with IBD treated with biologics. Institutional review board approval was obtained from each site for ongoing data collection and transfer. Data were collected individually by sites using a standardized

## What You Need to Know

### Background

Patients with Crohn's disease (CD), but not ulcerative colitis (UC), of shorter duration have higher rates of response to tumor necrosis factor antagonists than patients with longer disease duration, but little is known about the association between disease duration and response to other biologic agents. We analyzed data from patients with CD or UC treated with vedolizumab and used time to event analyses to compare rates of clinical remission, corticosteroid-free remission (CSFR), and endoscopic remission between patients with early-stage ( $\leq 2$  years duration) and later-stage ( $> 2$  years) CD or UC.

### Findings

Patients with CD for 2 years or less were significantly more likely to achieve a complete response, CSFR, or endoscopic response to vedolizumab than patients with longer disease duration. Disease duration did not associate with response vedolizumab in patients with UC.

### Implications for patient care

Patients given a diagnosis of CD should begin treatment with anti-TNF agent or vedolizumab as soon as possible.

data collection form and transferred (after deidentification) to the coordinating site (University of California, San Diego) for data compilation and analysis. The current analysis represents data collected between May 2014 and December 2016. The results of this study are reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology guidelines for cohort studies.<sup>12</sup>

### Variables

Data on variables of interest were collected including: patient characteristics (age at diagnosis, age at vedolizumab initiation, gender, smoking status, body mass index), disease characteristics (prior hospitalizations, prior surgeries, disease-related complications or extra-intestinal manifestations, and phenotype classified according to the Montreal classifications for CD and UC), and treatment history (steroids, immunomodulators, and TNF antagonists; duration of use; indication for discontinuation; and complications). Variables of interest specific to vedolizumab use were baseline disease severity (endoscopic, radiographic, or clinical assessments), concomitant treatments (steroids and/or immunomodulators), infusions (dates, intervals, premedications), and follow-up assessments (endoscopic, radiographic, or clinical assessments). Clinical assessments were classified as severe versus nonsevere based on physician

global assessment, where mild or moderate severity were classified as nonsevere. The primary variable of interest was disease duration, defined as a dichotomous variable. Shorter duration was defined as  $\leq 2$  years and longer duration as  $> 2$  years at the time of vedolizumab initiation. This definition is consistent with most prior data on the impact of disease duration on the efficacy of biologics.<sup>8,9</sup>

### Participants

Individuals were included in the current analysis if they met the following criteria: (1) confirmed diagnosis of CD or UC based on clinical and endoscopic or radiographic data, (2) active clinical symptoms attributed to CD or UC before starting vedolizumab, and (3) had at least 1 clinical and/or endoscopic follow-up after initiation of therapy. Patients started on vedolizumab for indeterminate colitis or pouchitis, or those in clinical remission at the time of starting vedolizumab (eg, patients with CD transitioned from natalizumab to vedolizumab for safety or initiated on vedolizumab for postoperative prophylaxis of CD) were excluded.

### Outcomes

The primary outcomes of interest were the cumulative rates for clinical remission, corticosteroid-free remission (CSFR), or endoscopic remission at 6 months. Timing of assessments for response followed routine practice standards as dictated by local sites with no predetermined or standardized time-point of assessment. Clinical assessments for remission were performed based on physician global assessment, where remission was defined as complete resolution of all CD- or UC-related symptoms by treating physician evaluation. The assessment of CSFR (performed only in patients on prednisone or budesonide at the time of initiation of vedolizumab) was defined as tapering off steroids completely, achieving clinical remission, and no repeat steroid prescription within 4 weeks of tapering. Endoscopic remission was defined as the absence of ulcers and/or erosions in CD or a Mayo endoscopic score of  $\leq 1$  in UC.<sup>13,14</sup> Endoscopic categorization was done by local study investigators and was reverified by a coordinating study investigator (P.S.D.) using deidentified endoscopy reports, with any discrepancies resolved through consensus between the study sites and the coordinating site.

### Statistical Analysis

Continuous variables were presented as means and standard deviations, or as medians and interquartile ranges based on data distribution. Categorical and binary variables were presented as proportions or percentages. For the comparison of baseline continuous variables, we used the independent sample *t* test (2 group comparisons)

or 1-way analysis of variance with Bonferroni correction (3 or more group comparisons). For the comparison of baseline binary variables, we used the Pearson chi-square or Fisher exact tests. Primary and secondary outcomes were described quantitatively with Kaplan-Meier survival and time-to-event analyses. Data were collected at clinical follow-up times determined by each treating physician, and 6-month cumulative outcomes were used in this study to maximize available data. A sensitivity analysis was performed by transforming disease duration into a categorical variable ( $\leq 2$  years,  $> 2$  years to  $\leq 5$  years, and  $> 5$  years), and outcomes were described quantitatively with Kaplan-Meier survival and time-to-event analyses to understand if the definition for early disease in CD could be extended to 5 years.

Cox proportional hazards regression analyses were performed to identify independent predictors of treatment outcomes. All baseline variables from the univariable analyses with a *P* value of  $< .20$  were fitted and a backward model selection approach was taken where the variable with the highest *P* value was sequentially selected out until all remaining variables in the model had a *P* value of  $< .05$ . Prior TNF antagonist exposure was included in all multivariable models, irrespective of *P* value. An assessment of interaction terms was then performed and interactions were retained if they had a *P* value of  $< .05$ .

Hazard ratios (HR) with 95% confidence interval (CI) are presented for independent predictors where  $HR < 1$  indicated a predictor was associated with a reduced probability for achieving the outcome and  $HR > 1$  indicated a predictor was associated with an increased probability for achieving the outcome. Two-sided *P* values  $< .05$  were considered statistically significant. Statistical analyses were performed using Stata statistical software (College Station, TX).

### Study Sponsor

Takeda Pharmaceuticals provided funding for statistical support to analyze the data. Takeda Pharmaceuticals and associated employees did not have access to any of the data, and all data analyses were performed at the University of California San Diego by the VICTORY Consortium investigators or statisticians.

## Results

### Crohn's Disease: Demographics

A total of 650 patients with CD were included. In the CD group, there were significant differences in baseline disease and treatment-related characteristics between those with disease duration  $\leq 2$  years and those with duration greater than 2 years (Table 1). Patients with longer disease duration had higher rates of CD-related complications including stricturing and penetrating disease (70% and 38% vs 39% and 23%, respectively;  $P < .05$  for both

**Table 1.** Baseline Demographics of Patient Cohorts

	CD			UC		
	≤2 y (n = 62)	>2 y (n = 588)	P value	≤2 y (n = 109)	>2 y (n = 328)	P value
Age, y, median (IQR)	29 (23–44)	37 (27–52)	.07	31 (24–52)	41 (29–57)	< .01
Male, n (%)	29 (47)	243 (41)	.42	57 (52)	161 (49)	.58
CRP, median (IQR)	3.1 (1–10)	5 (1–18)	.34	1.1 (0.4–5.4)	2.3 (0.7–7.8)	.36
Albumin, median (IQR)	4.0 (3.6–4.3)	3.9 (3.6–4.2)	.74	3.9 (3.6–4.3)	4.0 (3.7–4.3)	.16
BMI, median (IQR)	23.7 (20–28.8)	23.7 (21–28.6)	.71	23 (21.2–28)	25 (21.8–29)	.86
Hospitalized in previous year, n (%)	32 (52)	203 (34)	.01	28 (26)	82 (25)	.90
CD phenotype, n (%)						
Stricturing or penetrating disease	24 (39)	414 (70)	< .01			
Fistulizing disease	14 (23)	222 (38)	.02			
Prior surgery	22 (35)	377 (64)	< .01			
UC extent, n (%)						.23
E1				4 (4)	18 (5)	
E2				33 (30)	123 (38)	
E3				72 (66)	187 (57)	
Disease severity, severe, n (%)	21 (34)	202 (34)	.53	42 (39)	98 (30)	.06
Steroid refractory/dependent, n (%)	25 (40)	220 (37)	.68	56 (51)	152 (46)	.38
TNF antagonist failure, n (%)	37 (60)	455 (77)	< .01	61 (56)	185 (56)	1.00
Number of prior TNF antagonist agents, n (%)			< .01			.05
0	14 (23)	46 (8)		42 (38)	101 (31)	
1	27 (44)	128 (22)		51 (47)	144 (44)	
2+	21 (34)	414 (70)		16 (15)	83 (25)	
Concomitant steroids, n (%)	32 (52)	265 (45)	.35	65 (60)	174 (53)	.27
Concomitant IM, n (%)	19 (31)	251 (43)	.08	44 (40)	103 (31)	.10

BMI, body mass index; CD, Crohn's disease; CRP, C-reactive protein; IM, immunomodulator; IQR, interquartile range; TNF, tumor necrosis factor; UC, ulcerative colitis.

comparisons). A higher percentage of longer duration patients had failed TNF antagonists (77% vs 60%;  $P < .01$ ), and 70% of those in the longer disease duration group previously had failed at least 2 TNF antagonists versus 34% in the shorter disease duration group ( $P < .01$ ).

### Crohn's Disease: Cumulative Rates and Predictors of Remission

The cumulative rates for clinical remission, CSFR, and endoscopic remission for CD at 6 months were

significantly higher in the early disease duration group than in the longer disease duration group (Table 2, Figure 1). When further stratifying the long disease duration into >2 years to ≤5 years versus >5 years, no differences were seen between these 2 groups across any of the primary endpoints (Supplementary Figure 1).

On multivariable analyses for CD, disease duration ≤2 years remained a significant predictor of clinical remission (adjusted HR [aHR], 1.59; 95% CI, 1.02–2.49), CSFR (aHR, 3.39; 95% CI, 1.66–6.92), and endoscopic remission (aHR, 1.90; 95% CI, 1.06–3.39) (Table 3).

**Table 2.** Remission Rates at 6 Months Stratified by Disease Duration

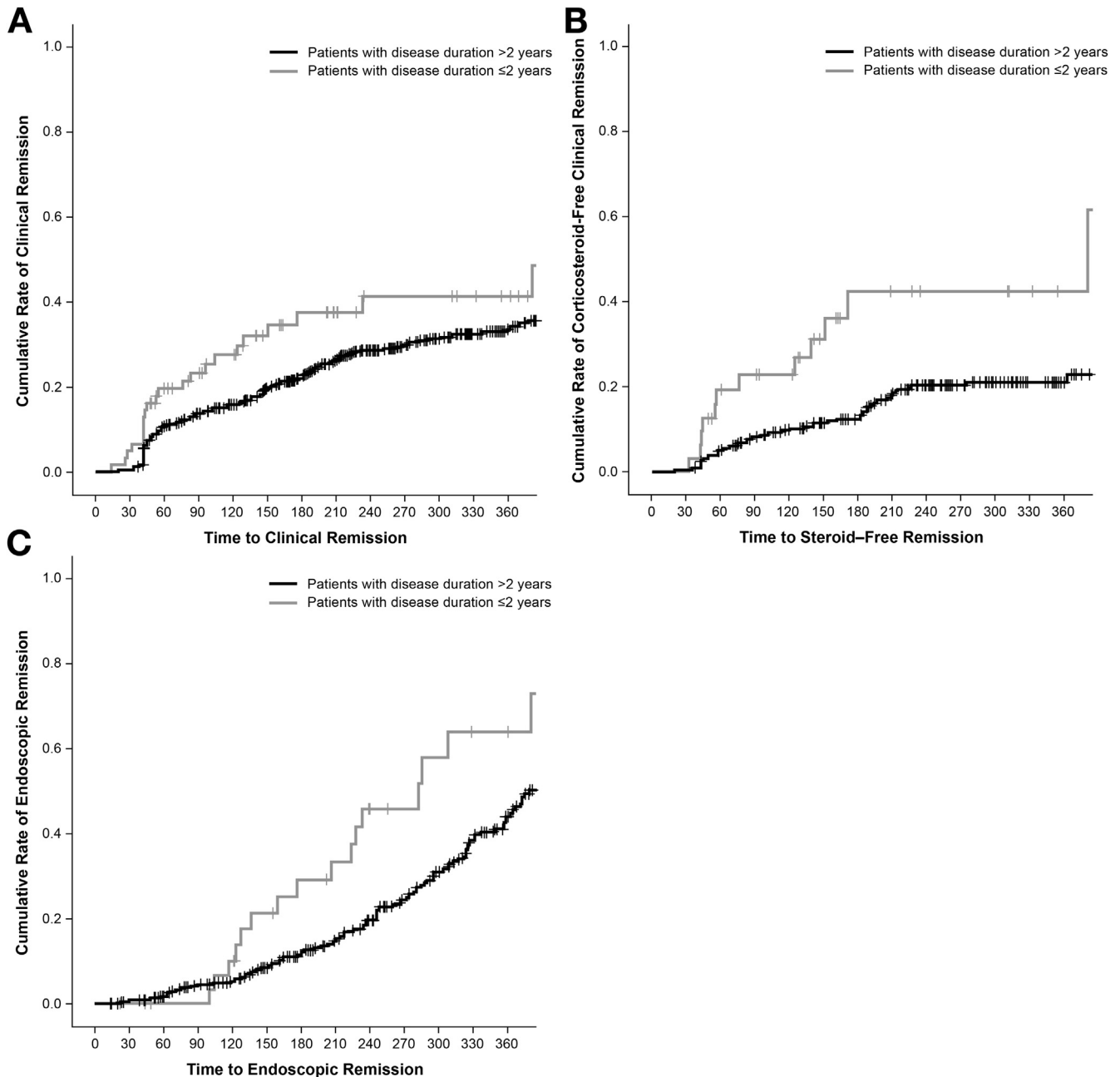
	Remission rates	
	≤2 y (n = 62)	>2 y (n = 588)
Crohn's disease		
Clinical remission, % <sup>a</sup>	38	23
Corticosteroid-free remission, % <sup>a</sup>	43	14
Endoscopic healing, % <sup>a</sup>	29	13
Ulcerative colitis	≤2 y (n = 109)	>2 y (n = 328)
Clinical remission, %	35	33
Corticosteroid-free remission, %	22	20
Endoscopic healing, %	16	22

<sup>a</sup>Significant ( $P < .05$ ) on log-rank analyses.

### Ulcerative Colitis: Demographics

A total of 437 patients with UC were included. In contrast to CD, there were few differences in baseline demographic characteristics between the early and longer disease duration of UC groups (Table 1). There was a comparable distribution of disease extent according to the Montreal classification between the 2 groups, a similar number of steroid-refractory or steroid-dependent patients, and a comparable percentage of TNF antagonist naive patients (44% in both groups). Notably, among those who had failed a prior TNF antagonist, there was a higher percentage of individuals in the longer disease duration group who had failed 2 or more TNF antagonist medications (25%





**Figure 1.** Cumulative rates of remission stratified by disease duration  $\leq 2$  years or  $> 2$  years. (A) Clinical remission. (B) Corticosteroid-free remission. (C) Endoscopic remission.

vs 15%;  $P = .05$ ) than in the shorter disease duration group.

#### *Ulcerative Colitis: Cumulative Rates and Predictors of Remission*

Among patients with UC, there were no significant differences in any of the outcomes between those with disease duration  $\leq 2$  years and those with longer disease duration (Table 2). Univariable and multivariable analyses were not performed for UC because initial time-to-event analyses revealed no differences in outcomes between early and longer disease duration groups.

## Discussion

In this multicenter consortium study, we observed that treatment with vedolizumab in the first 2 years after diagnosis of CD is associated with higher rates of clinical, corticosteroid-free, and endoscopic remission than treatment initiated later in the disease course. This improved treatment response was seen across all of the study endpoints in CD, and persisted after controlling for other predictors of treatment outcome, including prior TNF antagonist therapy. In contrast, no association between disease duration and treatment outcome was seen in patients with UC.

**Table 3.** Multivariable Predictors of Treatment Outcomes in Crohn's Disease

Predictors of treatment outcomes in Crohn's disease	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Clinical remission		
Structuring or penetrating phenotype	0.58 (0.44–0.77)	0.69 (0.51–0.92)
Disease severity (severe vs nonsevere)	0.40 (0.28–0.56)	0.53 (0.43–0.65)
Hospitalized in previous year	0.66 (0.49–0.90)	0.71 (0.52–0.97)
Disease duration ≤2 y	1.69 (1.09–2.61)	1.59 (1.02–2.49)
TNF antagonist exposure	0.51 (0.34–0.77)	0.64 (0.42–0.98)
Corticosteroid-free remission		
Albumin	1.47 (0.89–2.43)	1.76 (1.04–2.97)
TNF antagonist exposure	0.43 (0.22–0.85)	0.40 (0.20–0.80)
Disease duration ≤2 y	2.99 (1.59–5.64)	3.39 (1.66–6.92)
Endoscopic remission		
CRP	0.97 (0.96–0.99)	0.98 (0.96–0.99)
Albumin	2.29 (1.52–3.45)	1.70 (1.14–2.55)
Disease severity (severe vs nonsevere)	0.46 (0.32–0.66)	0.59 (0.45–0.77)
Disease duration ≤2 y	1.89 (1.12–3.18)	1.90 (1.06–3.39)
TNF antagonist exposure	0.63 (0.36–1.12)	0.95 (0.52–1.72)

NOTE. Variables entered in the multivariable models before backward selection was performed included those with  $P < .2$ . TNF antagonist exposure was included in all models irrespective of  $P$  value at each step. For clinical remission, variables included gender, hospitalized within previous 1 year, CRP, albumin, structuring/penetrating phenotype, fistulizing disease, disease severity, and concomitant steroids. For corticosteroid-free remission, variables included gender, CRP, albumin, fistulizing disease, and disease severity. For endoscopic remission, variables included hospitalized within previous 1 year, CRP, albumin, structuring/penetrating phenotype, fistulizing disease, disease severity, concomitant steroids, and combination therapy with immunomodulator. CI, confidence interval; CRP, C-reactive protein; HR, hazard ratio; TNF, tumor necrosis factor.

In recent years, there has been an intense interest in early, aggressive treatment of CD, to reduce the long-term morbidity associated with progressive bowel damage.<sup>15</sup> Early intervention is thought to target CD in a “window of opportunity” before irreparable bowel damage sets in.<sup>16</sup> A lower percentage of patients in our study in the early CD group had fistulizing or penetrating complications, which supports this hypothesis. A second theory invokes different immune responses in early versus late CD,<sup>17</sup> including differential T-cell immune responses to interleukin-12 stimulation in children with early versus late CD<sup>18</sup> and increases in peripheral T-helper cell type 17 cells in patients with late versus early CD.<sup>19</sup> Finally, the microbiome plays an important role in responsiveness to therapy in IBD,<sup>20</sup> and treatment-naive early IBD may have a distinct microbiota composition that can impact therapy outcomes.<sup>21</sup>

The landmark “Step-up/Top-down” study<sup>22</sup> was the first to show in a randomized controlled trial that early aggressive therapy with combined infliximab and azathioprine was superior to conventional step-up approach in early CD for achieving early remission. Similarly, a post hoc analysis of the landmark SONIC trial<sup>23</sup> stratifying by disease duration demonstrated higher efficacy in achieving rigorous endpoints, such as a composite of clinical remission, mucosal healing, and C-reactive protein normalization in patients with CD treated within 18 months of diagnosis.<sup>24</sup> Similar findings have been found with adalimumab and certolizumab monotherapy in early CD.<sup>8,9</sup> In contrast to TNF antagonist medications, immunomodulators have not been shown to be more effective in early disease in achieving remission and mucosal healing.<sup>25,26</sup>

Our data add to the growing literature on early intervention in CD and demonstrate that improved outcomes with early treatment are not a limited class effect of TNF antagonist therapy. Importantly, this effect was seen even in a relatively refractory cohort, with 60% of patients with CD treated early with vedolizumab already having failed at least 1 TNF antagonist. This finding represents an important step in targeting disease modification in CD, because vedolizumab has also been shown to have an excellent safety profile,<sup>27,28</sup> although studies with long-term follow-up are still needed. Therefore, while balancing the benefits of early intervention with the possible side effects of increased duration of drug exposure, vedolizumab may be an excellent candidate for early initiation.

In contrast to the emerging literature on the benefits of early intervention in CD, there is a paucity of data on early intervention in UC, and whether UC is a progressive disease like CD remains unclear. In a retrospective cohort study of the early initiation of infliximab or adalimumab within 3 years of UC diagnosis, Ma et al<sup>29</sup> found no difference in the rates of UC-related hospitalizations, secondary loss of response, or colectomy between early and late treatment groups. Similarly, Mandel et al<sup>30</sup> found that early TNF antagonist use in CD, but not in UC, was associated with decreased hospitalization rates. We are also unaware of any post hoc analyses of clinical trials in UC demonstrating any impact of disease duration on treatment efficacy. Our data are consistent with these prior retrospective studies in showing no difference between early and late initiation of vedolizumab on short-term treatment outcomes in UC.

The reason for the differing impact of early treatment in UC versus CD is not clear. One hypothesis is that



demonstration of disease modification in UC may require a longer duration of follow-up. The risk of colorectal malignancy has been shown to correlate with the intensity and longevity of endoscopic and histologic intestinal inflammation,<sup>31</sup> and therapy that can effectively promote and maintain mucosal healing may decrease the long-term risk of colorectal cancer.<sup>32–35</sup> Histologic healing as an independent endpoint has garnered significant attention in recent years<sup>36,37</sup> and would be an interesting endpoint for future evaluation in our cohort. Similarly, chronic inflammation leading to bowel damage and fibrosis in UC may yield poorer functional outcomes because of loss of luminal wall compliance and development of anorectal dysfunction and motility disorders.<sup>32,38</sup> Whether early intervention with vedolizumab and other agents can alter the natural history of UC and prevent these complications needs to be explored further in longitudinal studies.

The strengths of our study include the large, real-world, multicenter data set that represents a broad population of individuals with IBD. Patients had detailed clinical and endoscopic data collected using standardized extraction methods. Our data are concordant with studies of TNF antagonist medications in early IBD showing a benefit in early CD but not UC, but importantly we extend these findings to vedolizumab, which has not previously been observed.

Our study does have several important limitations. The retrospective collection of data across multiple institutions and the lack of well-validated clinical indices for measuring treatment remission may impact response estimates. Additionally, no central reading of endoscopies was performed, but rereview of reports by a single study investigator resulted in <5% reclassification of endoscopic scoring. Furthermore, the follow-up time used for the primary outcomes in this study was relatively short and the rates of additional outcomes, such as surgeries and hospitalizations, were too low for meaningful analysis. Further data collection is needed to assess the durability of the improved response rates in the treatment of early CD, and to assess for a possible impact on long-term outcomes in UC. Finally, important differences exist in the disease phenotype and treatment experience of the early versus late groups, especially in CD. Despite rigorous multivariable modeling to control for these factors, there remains the possibility of unmeasured confounders impacting response and remission rates.

In summary, we found that vedolizumab-treated patients with CD with early disease ( $\leq 2$  years) had significantly improved outcomes with higher rates of clinical, corticosteroid-free, and endoscopic remission than those with longer disease duration. In contrast, this improvement was not seen in patients with UC with short disease duration treated with vedolizumab. The combined safety and efficacy of vedolizumab makes it an attractive candidate for early, aggressive intervention in hopes of achieving lasting disease modification. Further studies are needed to explore the impact of early use of

vedolizumab on long-term outcomes and its ability to prevent disease progression in CD and UC.

## Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at [www.cghjournal.org](http://www.cghjournal.org), and at <http://doi.org/10.1016/j.cgh.2018.12.040>.

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#### Reprint requests

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#### Conflicts of interest

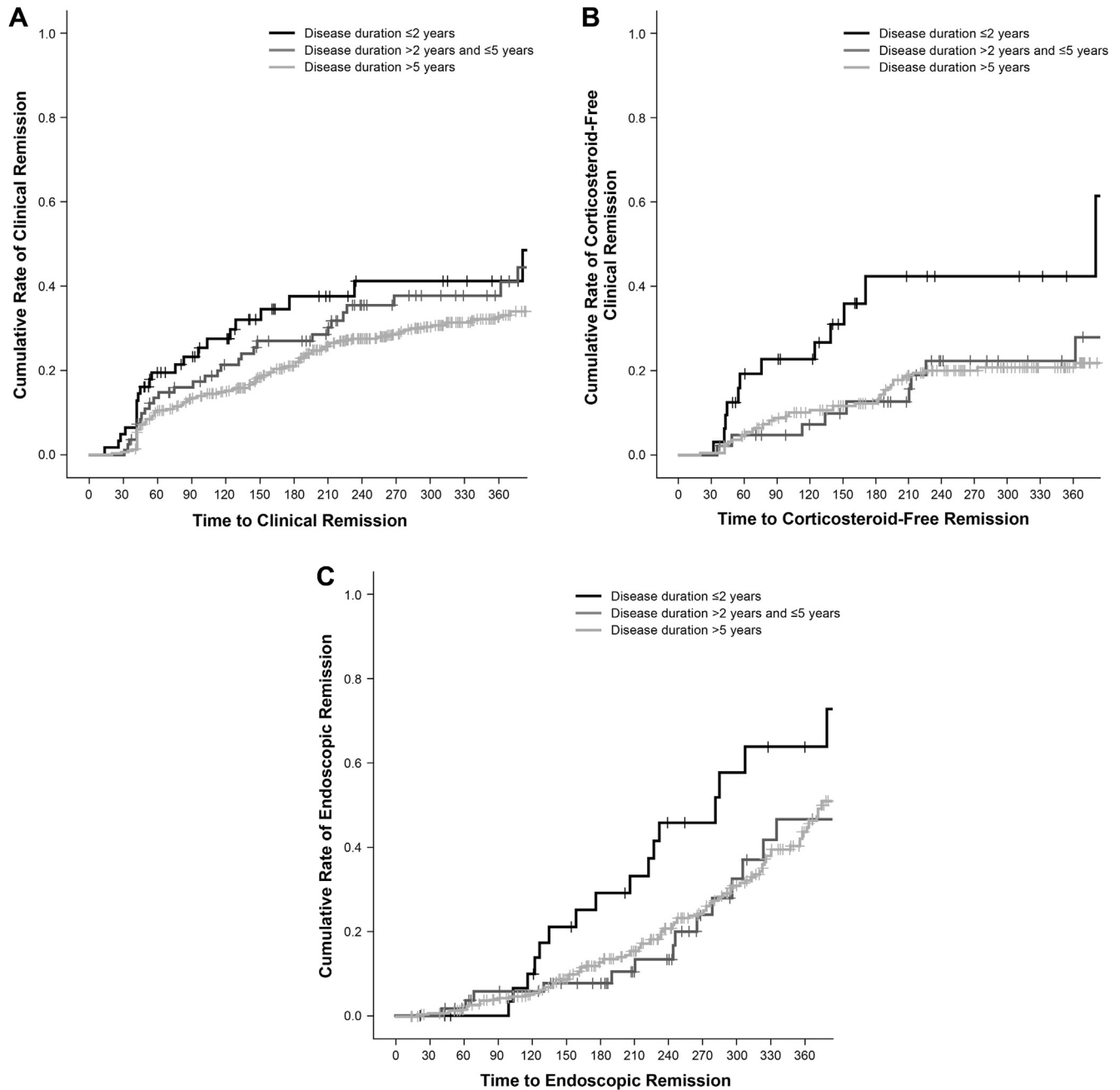
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**Supplementary Figure 1.** Cumulative rates of remission stratified by disease duration  $\leq 2$  years,  $> 2$  to  $\leq 5$  years,  $> 5$  years. (A) Clinical remission ( $P = .01$  for  $\leq 2$  vs  $> 5$  years;  $P > .10$  for all other comparisons). (B) Corticosteroid-free remission ( $P < .01$  for  $\leq 2$  vs  $> 5$  years and  $P = .02$  for  $\leq 2$  vs  $> 2$  to  $\leq 5$  years;  $P > .10$  for all other comparisons). (C) Endoscopic remission ( $P = .02$  for  $\leq 2$  vs  $> 5$  years and  $P = .05$  for  $\leq 2$  vs  $> 2$  to  $\leq 5$  years;  $P > .10$  for all other comparisons).