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Original Article

The Effect of Vedolizumab on Spondyloarthritis Symptoms in a Cohort of Inflammatory Bowel Disease Patients

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Abstract

Objective: Vedolizumab is a novel anti-inflammatory molecule that is currently being used in the treatment of refractory inflammatory bowel disease. The mode of action is inhibiting the binding of activated T lymphocytes to the adhesion molecule 1 of intestinal mucosal cells. Due to its local effect, systemic immunosuppression is not expected, and this may have a negative effect on the extra-intestinal symptoms of inflammatory bowel disease, particularly spondyloarthritis. Currently, there is limited data regarding the effect of vedolizumab on spondyloarthritis symptoms. We aimed to investigate whether vedolizumab has an effect on the occurrence of rheumatological symptoms and the clinical course of patients who have spondyloarthritis.

Methods: Thirty-nine adult inflammatory bowel disease patients who were followed up in the Gastroenterology Clinic and treated with vedolizumab were included in the study. Patients were reviewed in terms of rheumatological manifestations. The occurrence of new musculoskeletal findings during the vedolizumab treatment was recorded. Patients with a former diagnosis of spondyloarthritis were evaluated for the activity of axial and peripheral manifestations during the vedolizumab.

Results: There were 39 inflammatory bowel disease patients (29 Crohn's disease, 10 ulcerative colitis, 48.7% (n = 19) male) who had been treated with vedolizumab. The mean age of the patients was 41.4 ± 15.7 years, and the duration of inflammatory bowel disease was 10.4 ± 7.5 years. A total of 17 (44%) patients had accompanying spondyloarthritis findings (mean age 47.08 ± 15.325 years and 58.8% M). Seven patients had axial dominant symptoms and 6 of them were in an active disease state before vedolizumab. During vedolizumab, all but 1 continued to be active. There were 14 patients with arthritis/arthralgias before vedolizumab and only 3 had improvement with therapy. On the other hand, there were 3 patients who had new-onset arthralgias/arthritis with vedolizumab. In total, 6 patients needed to stop vedolizumab because of spondyloarthritis activation (n = 2) and uncontrolled inflammatory bowel disease (n = 4), respectively.

Conclusion: Treatment with vedolizumab seems no effect on both the occurrence and the course of rheumatological manifestations in inflammatory bowel disease patients. Further studies are required to replicate our results.

Keywords: Vedolizumab, tumor necrosis factor inhibitors, inflammatory bowel diseases, spondyloarthritis, ankylosing spondylitis

Introduction

Spondyloarthritis (SpA) is an umbrella term that groups heterogeneous diseases sharing some common clinical, laboratory, imaging, and genetic features. The prototype and the most common form of SpA is ankylosing spondylitis (AS). Enteropathic arthritis (EA) is a rare form of SpA that is seen in patients with inflammatory bowel disease (IBD).[1] The overlap between IBD and SpA sometimes becomes a challenging issue while treating patients. The use of non-steroid anti-inflammatory drugs (NSAIDs) and their potential effect on flaring up the underlying IBD[2] and the inefficacy of tumor necrosis factor-alpha inhibitory (TNFi) treatments other than monoclonal antibodies[3] and interleukin (IL) 17 targeting treatments such as secukinumab in IBD patients limit the available therapeutic options for EA.[4] Vedolizumab (VDZ) is a humanized monoclonal antibody that is used for the treatment of refractory IBD as a second- or third-line choice. It shows its anti-inflammatory effect locally by binding to integrin and preventing leukocyte binding to the endothelial surface.[5,6] Studies addressing VDZ and its effect on SpA are limited. When considering the unmet need in the treatment of SpA, we, therefore, studied the effect of VDZ in patients with EA.

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Methods

Adult IBD patients who had been treated with VDZ and registered in the IBD clinic were identified. These patients were contacted by phone and scheduled for an interview with a rheumatologist on their next IBD outpatient clinic visit. During that visit, patients were investigated thoroughly with regard to the SpA-related symptoms. The following data were collected: (i) former diagnosis of SpA by rheumatologist, (ii) the presence of inflammatory back pain (IBP) based on Calin criteria,[7] (iii) presence of arthritis, enthesitis, dactylitis, uveitis, psoriasis, and family history of SpA, (iv) the assessment of the sacroiliac joints (SIJs) from the latest available pelvic x-rays and abdominal computed tomography (CT) based on the modified New York criteria[8] and Chan scoring system,[9] respectively. If available, inflammatory changes on SIJs by magnetic resonance imaging (MRI) were recorded,[10] and (v) laboratory tests including erythrocyte sedimentation rate, C-reactive protein, and HLA-B27 were noted. Patients were then classified into the axial[11] and peripheral[12] SpA subtypes as defined by the Assessment in SpondyloArthritis international Society (ASAS) group. For patients who did not satisfy ASAS classification but had SpA-related findings, we used the term undifferentiated SpA (uSpA).[13] Patients were then grouped into the following categories: (i) patients with a current diagnosis of SpA, (ii) patients newly diagnosed as SpA, and (iii) IBD patients without SpA. For imaging, 2 experienced readers (IS and AB) scored the available CTs and discordant results settled through the consensus.

The clinical classification of IBD was used by Montreal criteria.[14] Disease activity of Crohn's disease (CD) and ulcerative colitis (UC) was assessed by the CD activity index[15] and clinical activity index according to Rachmilewitz,[16] respectively. Former and current therapies for IBD patients were noted. Ethical approval for this study was obtained from the ethics committee of Dokuz Eylül University, and all participants gave written informed consent for participating in the study (Decision No: 2021/10-45).

Main Points

- Vedolizumab (VDZ) treatment has no effect on axial and peripheral symptoms in spondyloarthritis (SpA) patients.
- Paradoxical arthritis related to VDZ is not an expected symptom.
- Spondyloarthritis prevalence in refractory inflammatory bowel disease (IBD) patients is 43.5% and 18% of the IBD patients had no SpA symptoms despite the unequivocal radiographic changes in sacroiliac joints, and about 10% of the SpA patients needed to stop VDZ as because of flare.

Statistical Analysis

The Kolmogorov–Smirnov normality test was used to determine the distribution pattern of the variables. Continuous variables were presented as mean ± standard deviation (SD) and nominal and ordinal data were expressed as percentages. Kappa statistic was used to analyze the reliability of identifying sacroiliitis on CT between readers. The statistical analysis was carried out by using Statistical Package of Social Sciences Version 22.0. (IBM SPSS Corp.; Armonk, NY, USA).

Results

General Characteristics of the Study Patients

There were 39 patients who had been treated with VDZ (CD = 29 (74.4%) and UC = 10 (25.6%)). The mean age and disease duration of the patients were 41.4 ± 15.7 and 10.4 ± 7.5 years, respectively, and 19 (48.7%) of them were male. Based on the Montreal classification, L3 (62.1%) and E3 (60%3) were the most frequent locations for CD and UC, respectively. Fourteen (35.9%) patients had required surgical intervention for IBD. The medications prior to VDZ were as follows: 5 aminosalicylic acid (100%), systemic corticosteroids (94.9%), azathioprine (84.6%), infliximab (87.2%), adalimumab (79.5%), budesonide (51.3%), methotrexate (28.2%), certolizumab pegol (12.8%), NSAIDs (12.8%), and secukinumab (2.6%). Based on the latest available clinical visit, while 33 (84.6%) patients were continuing VDZ, 6 (15.4%) had to stop their medication for various reasons. The mean use of VDZ was 104 ± 72.5 weeks.

Rheumatological Manifestations of the Patients

In total, 17 (43.5%) patients had SpA-related symptoms and findings. The mean age and disease duration of the patients were 47.1 ± 15.3 years and 13 ± 6.4 months, respectively, and 10 (58.8%) were male. The dominant findings were peripheral in 2 (11.8%), axial in 9 (52.9%) and both peripheral and axial in the remaining 6 (35.3%) patients. Nine (52.9%) out of 17 patients had a former diagnosis of SpA and 8 patients were newly diagnosed. Among them, 1 patient had an IBP and 7 had imaging findings (from abdominal CT) without SpA symptoms. Agreement on CT scoring based on Kappa statistics between the observers was 0.75. When patients were grouped into the novel classification criteria, 4 (23.5%) were fulfilling ASAS axial, 8 (47.1%) were satisfying ASAS peripheral, and 7 (41.1%) were in the uSpA category. Inflammatory back pain according to the Calin criteria was present in 7 (41.2%) patients. The clinical characteristics of the SpA patients are given in Table 1.

When imaging findings were analyzed, there were 6 (35.3% in SpA and 15.4% in the total group) patients who had sacroiliitis according to the mNYc (2 had bilateral grade 2 and others unilateral or bilateral grade 3 or 4). All IBD patients had abdominopelvic CT imaging during or prior to (maximum a year) VDZ therapy that was performed mainly for IBD-related reasons. The evaluation of SIJs based on the Chan scoring system revealed that 14 (82.3% in SpA and 35.9% in the total group) had sacroiliitis. There were only 4 patients who had SIJ MRI and 2 had active inflammation according to ASAS criteria. In the total group, HLA-B27 was tested in 6 patients and all were found to be negative. All former diagnosed SpA patients (n = 9) had been treated with at least 1 monoclonal TNFi prior to the VDZ. Two of these patients had to receive another monoclonal TNFi for the active SpA symptoms.

Aside from SpA, 1 patient was diagnosed as Sjogren's syndrome (2.6%) and the other was diagnosed as seronegative rheumatoid arthritis (2.6%). None of these patients had clinical or imaging symptoms compatible with SpA.

Effect of Vedolizumab on Spondyloarthritis Symptoms

There were 7 patients who have axial symptoms and 6 of these patients had severe back pain. During VDZ therapy, 5 (83.3%) patients reported that back pain intensity did not change, 1 (16.7%) patient's back pain improved, and the other one who did not have axial symptoms started having back pain. In total, 6 (85.7%) out of 7 patients with axial symptoms were having severe back pain during VDZ.

Arthritis (8 patients) and arthralgias (5 patients) was present in 13 (33.3%) IBD patients before VDZ therapy. Eight of these patients had a diagnosis of former SpA (6 patients had arthritis; the arthritis pattern was oligoarticular in 4, polyarticular and monoarticular in 1 patient). During VDZ treatment, these patients continued to have joint symptoms and 3 (7.7%) additional patients without joint symptoms reported new-onset arthritis (1 patient; oligoarticular) and arthralgias (2 patients) during VDZ (Supplementary Table 1). The mean onset of arthritis/arthralgias was 14.1 ± 17.2 weeks

Table 1. The Clinical Characteristics of the SpA Patients

	Age, Sex	IBD Type, Duration (Years), Montreal Classification	SpA Subgroup	Sacroiliitis (CT/Radiography/ MRI)	Treatments Before VDZ	Peripheral Arthritis/ Arthralgia/IBP Before VDZ (ever)	Peripheral Arthritis/ Arthralgia/IBP During VDZ	VDZ Duration (Months)/ Discontinuation of VDZ	MSK Manifestations After VDZ
1	67, M	CD/5/L3-B2	uSpA	CT (+), x-ray —1/2	NSAID, 5-ASA, systemic steroid, AZA, IFX, ADA	–/–/–	–/–/–	11/–	-
2	53, F	CD/13/L3	pSpA	CT (+), x-ray—1/2, MRI (+)	5-ASA, systemic steroid, AZA, IFX, ADA, CTZ, MTX	+/–/– oligoarthritis	–/–/–	26/–	-
3	54, M	CD/5/L4	AxSpA	CT (+), x-ray—2/2	5-ASA, systemic steroid, AZA, IFX, ADA	–/–/+	–/–/+	24/–	No improvement in BP
4	39, F	CD/7/L3	pSpA	CT (+), x-ray—1/1	5-ASA, systemic steroid, IFX, ADA, CTZ, MTX	+/+/+ Monoarthritis	–/–/–	36/–	-
5	66, F	CD/19/L3-B3	uSpA	CT (+), x-ray—1/1	5-ASA, AZA, IFX, ADA	–/–/–	–/–/–	8/–	-
6	24, F	CD/4/L3	pSpA	CT (+), x-ray—1/3	5-ASA, systemic steroid, AZA, IFX, ADA, MTX	+/+/– Oligoarthritis	+/+/– Oligoarthritis	19/IBD unresponsiveness	Arthritis persisted
7	56, F	CD/9/L3	pSpA	CT (–), x-ray—0/0	5-ASA, systemic steroid, IFX, ADA, MTX	+/ +/– Oligoarthritis	–/–/–	13/–	-
8	49, F	CD/12/L3-B3-P	AxSpA, pSpA	MRI (+)	NSAID, 5-ASA, systemic steroid, AZA, IFX, ADA, MTX	+/+/+ Oligoarthritis	–/+/+	41/–	No improvement in BP
9	69, M	UC/17/E3	uSpA	CT (+), x-ray—3/3	5-ASA, systemic steroid, AZA, IFX, ADA, MTX	–/–/–	+/+/+ Oligoarthritis	24/–	Arthritis improved after MTX
10	59, M	CD/9/L2	uSpA	CT (+), x-ray—2/1	5-ASA, IFX, CTZ, MTX	–/+/–	–/+/–	36/–	-

(*Continued*)

Table 1. The Clinical Characteristics of the SpA Patients (*Continued*)

	Age, Sex	IBD Type, Duration (Years), Montreal Classification	SpA Subgroup	Sacroiliitis (CT/Radiography/MRI)	Treatments Before VDZ	Peripheral Arthritis/Arthralgia/IBP Before VDZ (ever)	Peripheral Arthritis/Arthralgia/IBP During VDZ	VDZ Duration (Months)/Discontinuation of VDZ	MSK Manifestations After VDZ
11	50, M	UC/4/E3	pSpA	CT (+), x-ray—1/3	5-ASA, systemic steroid, AZA, IFX, ADA	+/–/– Oligoarthritis	–/–/–	11/–	-
12	24, M	CD/15/L3	uSpA	CT (+), x-ray—2/1	5-ASA, systemic steroid, AZA, IFX, ADA	–/–/–	–/–/–	15/–	-
13	47, M	CD/12/L3	uSpA	CT (+)	5-ASA, systemic steroid, IFX, ADA	–/–/–	–/–/–	12/–	-
14	40, M	CD/2/L3	AxSpA	CT (+), x-ray—3/3	NSAID, 5-ASA, systemic steroid, IFX, ADA	–/–/+	–/+/+	3/SpA Flare	Improvement in BP
15	26, F	CD/6/L3	pSpA	CT (–), x-ray—0/0	NSAID, 5-ASA, systemic steroid, IFX	+/+/+ Oligoarthritis	–/+/+	13/IBD unresponsiveness	No improvement in BP
16	54, F	CD/28/L3	AxSpA, pSpA	CT (+), x-ray—2/2	NSAID, 5-ASA, systemic steroid, IFX, MTX	+/+/+ Polyarthritis	+/+/+ Polyarthritis	2 weeks/IBD unresponsiveness + arthritis	DMARD for arthritis, no improvement in BP
17	23, M	CD/12/E2	uSpA	CT (+)	5-ASA, systemic steroid, AZA, IFX, ADA	–/+/+	–/+/+	6/IBD unresponsiveness	-

ADA, adalimumab; AxSpA, axial spondyloarthritis based on ASAS; AZA, azathioprine; BP, back pain; CD, Crohn's disease; CT, computed tomography; CTZ, certolizumab; DMARD, disease-modifying antirheumatic drugs; F, female; IBD, inflammatory bowel disease; IBP, inflammatory back pain; IFX, infliximab; M, male; MRI, magnetic resonance imaging; MSK, musculoskeletal; MTX, methotrexate; NSAID, nonsteroidal anti-inflammatory drugs; pSpA, peripheral spondyloarthritis based on ASAS; UC, ulcerative colitis; uSpA, undifferentiated spondyloarthritis; VDZ, vedolizumab; 5-ASA, 5-aminosalicylic acid.

after the treatment. Supplementary Table 2 summarizes the SpA symptoms and their relation with VDZ therapy, and Table 2 demonstrates the relationship between IBD and SpA disease activities.

Summary of the Patients Who Discontinued the Vedolizumab

There were 6 (15.4%, 66.6% male, all with CD) IBD patients who needed to discontinue VDZ. Five out of 6 patients had SpA diagnosis. Four patients stopped their treatments because of active IBD and 2 (11.7% of the total SpA group) of them for active SpA.

Discussion

In this study, we showed the following: (i) VDZ treatment has no effect on axial and peripheral symptoms in SpA patients, (ii) paradoxical arthritis related to VDZ is not an expected symptom, (iii) SpA prevalence in refractory IBD patients is 43.5%, (iv) 18% of the IBD patients had no SpA symptoms despite the unequivocal radiographic changes in SIJs, and (v) about 10% of the SpA patients needed to stop VDZ as because of flare.

The prevalence of EA in the general population is about 0.01%.[17] The article published by de Winter et al[18] compared AS and non-radiographic axial SpA. It was stated "pooled analysis showed an IBD prevalence of 4.1% (CI: 2.3%-6.5%) in AS and 6.4% (CI: 3.6%-9.7%) in nr-axSpA, resulting in a pooled prevalence difference of 1.4% (CI −0.1% to 2.9%) favoring AS".[18] When patients with IBD are analyzed

Table 2. The Relationship Between IBD and SpA Disease Activity Status and SpA Symptoms

During VDZ Treatment		IBD Active; n (%)		IBD Inactive; n (%)	
		CD	UC	CD	UC
SpA active	Axial symptoms	2 (66.7)	-	1 (33.7)	-
	Peripheral symptoms	1 (100)	-	-	-
	Axial+ peripheral symptoms	3 (75)	1 (25)	-	-
SpA inactive	Axial symptoms	-	-	5 (100)	-
	Peripheral symptoms	-	-	1 (100)	-
	Axial+ peripheral symptoms	-	-	2 (66.7)	1 (33.3)

CD, Crohn's disease; IBD, inflammatory bowel disease; SpA, spondyloarthritis; UC, ulcerative colitis; VDZ, vedolizumab.

separately, clinical findings of SpA are reported between 1% and 10%, and radiological findings of SpA are present in about 20% to 50% of the patients.[19] In the current study, clinical findings of SpA were present in nearly 40% of the refractory IBD patients. This prevalence figure is obtained by a thorough investigation of the SpA findings by a rheumatologist. Before that, only 20% of the patients had a previous diagnosis of SpA suggesting an underestimation of SpA findings among the IBD group. Interestingly, despite the overt radiographic sacroiliitis, the majority of these undiagnosed patients almost had no apparent axial symptoms. When taken into account the severity of IBD in this group, the symptoms of bowel disease may overweigh the rheumatic symptoms. Another explanation for silent sacroiliitis may be the use of biologic drugs early in the disease course. This might probably suppress the inflammation and therefore axial disease. As the substantial number of patients remained undiagnosed, this finding highlights the importance of collaboration between gastroenterologists and rheumatologists in the management of EA.

Currently, compared with rheumatoid arthritis, the therapeutic armamentarium of SpA is limited. The first-line treatment for controlling axial symptoms is the use of NSAIDs.[20] However, NSAIDs and their negative effect on the gastrointestinal system are the main disadvantages of these medications. Available data suggested that up to 30% of the patients using NSAIDs reported dyspeptic complaints and about 70% of the long-term NSAID users had endoscopic abnormalities such as erosion, ulceration, or subepithelial bleeding.[21] The use of NSAIDs in IBD patients is another challenging issue. Some studies[22,23] suggested an increased risk of IBD flare-ups after the NSAIDs while others, including meta-analysis, did not support an activation, particularly with the use of selective Cox-2 inhibitors.[24-26] Therefore, these contradictions about NSAIDs limit the available therapeutic options for SpA in a substantial number of patients. In our cohort, nearly 15% of the patients reported NSAID usage. In line with this, a large-scale study suggested that 40% of IBD patients were using NSAIDs when needed.[27] Taken together with our findings, despite the risk of IBD activation, it may not be possible to limit NSAIDs in IBD. The use of TNFi has given new insights into the treatment of SpA particularly for patients who are refractory or have contraindications to the NSAIDs. Currently, all 5 TNFi are approved for the treatment of active axial and peripheral symptoms in SpA. Blocking TNF is also effective in controlling disease activity in IBD. In this respect, treatment with monoclonal antibodies such as infliximab and adalimumab is approved for both UC and CD; golimumab for UC and certolizumab for CD patients.[28] On the other hand, controlled trials failed to show an effect of etanercept on IBD.[29] Therefore, the type of associated bowel disease and the lack of effectiveness of etanercept on IBD significantly affect the therapeutic choice in SpA. Blocking IL-17 is also an effective treatment option in active SpA, but these medications did not have an effect on IBD. Furthermore, there is also a concern about the potential activation of underlying bowel disease as IL-17 is thought to have a role in the protection of epithelial barriers in the gut mucosa.[30,31] However, large-scale cohort studies and the extension phase of controlled trials failed to support this hypothesis suggesting a neutral effect of IL-17 inhibitors on IBD.[32] When considering about 40% of SpA patients may have a failure to biologic therapies, and the restrictions on the use of some of the medications as described previously, there is a substantial unmet need in the treatment of EA patients. In this regard, VDZ is filling an important gap in the treatment of refractory IBD. Although it is showing its effect locally, its effect on SpA symptoms is also of interest. Currently, there are no controlled trials investigating the VDZ and its effect on SpA symptoms such as axial pain and arthritis. Available data are limited to the case series,[33] post-hoc analysis of controlled trials,[34] and retrospective analysis of the cohort studies.[35] Some reported exacerbation of SpA symptoms after VDZ,[33,36] some reported a benefit in both axial and peripheral symptoms including enthesitis during VDZ,[37-39] and some did not show any relation with VDZ treatment and SpA activity.[40] Post-hoc analysis of OBSERV-IBD cohort reported new-onset arthritis/arthralgias in 14% of the patients receiving VDZ. In contrary, 47 patients with inflammatory arthralgia/arthritis present at baseline, nearly half of them had complete remission, while 20% did not have a symptomatic benefit. It was of note that about one-third of arthritis/arthralgia patients needed to stop the treatment for peripheral symptoms.[41] In the randomized controlled GEMINI trial, the frequency of arthralgia (13.3% vs. 13.5%) and back pain (4.0% vs. 4.7%) was similar between VDZ and placebo groups.[5] In the current study, about 80% of the patients who reported axial symptoms continue to be symptomatic after 62.2 $\pm$ 49.2 months of VDZ treatment. On the other hand, there was no benefit on patients who have arthritis and there were additional 3 patients with new-onset articular symptoms during the VDZ. Importantly, about 30% of the patients who needed to discontinue VDZ was stopped the medication because of active SpA.

As also noted in our study, VDZ has neutral effects on SpA manifestations, and some patients may need to discontinue their treatments for active rheumatological disease. In the literature, a combination of biologics and VDZ had been helpful for refractory EA patients suggesting that this approach may be served as an alternative solution for selected patients.[35]

We acknowledge our limitations as follows: (i) as the majority of these patients did not have a former diagnosis, specific disease activity and outcome measures for SpA such as the Bath AS disease activity index[42] could not be used and (ii) the relatively small number of patients, restricting the statistical power could also be considered as a limitation. However, considering the shortage of data regarding the effect of VDZ on SpA and limited number of studies reflecting real-life data, we think that our findings could provide additional information for clinicians and researchers studying this topic.

In conclusion, VDZ treatment seems no effect on the musculoskeletal manifestations of EA.

Undiagnosed SpA among patients with IBD is still a significant problem that needs close collaboration with rheumatology and gastroenterology. Unmet need in the treatment of EA is a significant problem, and further exploratory studies may shed light on whether locally effective drugs such as VDZ could be used with other biologics. Long-term studies and more data are needed to determine whether VDZ has an effect on the occurrence of new-onset SpA manifestations.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of Dokuz Eylul University (Approval No: 2021/10-45).

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Supplementary Table 1. New Onset Arthritis/Arthralgias During VDZ

	In All Patients (n = 39)	In Patients with Signs of SpA (n = 17)
Before VDZ (−) and during VDZ (+)	3 (7.6%)	2 (11.7%)
Before VDZ (+) and during VDZ (+)	11 (28.2%)	6 (35.2%)
Before VDZ (+) and during VDZ (−)	5 (12.8%)	3(17.6%)

SpA, peripheral spondyloarthritis; VDZ, vedolizumab.

Supplementary Table 2. SpA Symptoms and Their Relation with VDZ Therapy

		Before VDZ Treatment; n (%)	During VDZ Treatment; n (%)
AxSpA symptoms	Present	3 (33.3)	3 (37.5)
	Absent	6 (66.7)	5 (62.5)
pSpA symptoms	Present	2 (100)	1 (50)
	Absent	0 (0)	1 (50)
AxSpA + pSpA symptoms	Present	4 (66.6)	4 (57.1)
	Absent	2 (33.4)	3 (42.9)

AxSpA, axial spondyloarthritis; pSpA, peripheral spondyloarthritis; VDZ, vedolizumab.