Effectiveness and Safety of Mepolizumab in Combination with Corticosteroids in Patients with Eosinophilic Granulomatosis with Polyangiitis

Masanobu Ueno
University of Occupational and Environmental Health Japan: Sangyo Ika Daigaku
Ippei Miyagawa
University of Occupational and Environmental Health Japan: Sangyo Ika Daigaku
Kazuhisa Nakano
University of Occupational and Environmental Health Japan: Sangyo Ika Daigaku
Shigeru Iwata
University of Occupational and Environmental Health Japan: Sangyo Ika Daigaku
Kentaro Hanami
University of Occupational and Environmental Health Japan: Sangyo Ika Daigaku
Shunsuke Fukuyo
University of Occupational and Environmental Health Hospital: Sangyo Ika Daigaku Byoin
Satoshi Kubo
University of Occupational and Environmental Health Japan: Sangyo Ika Daigaku
Yusuke Miyazaki
University of Occupational and Environmental Health Japan: Sangyo Ika Daigaku
Akio Kawabe
University of Occupational and Environmental Health Japan: Sangyo Ika Daigaku
Hiroko Yoshinari
University of Occupational and Environmental Health Japan: Sangyo Ika Daigaku
Shingo Nakayamada
University of Occupational and Environmental Health Japan: Sangyo Ika Daigaku
Yoshiya Tanaka (tanaka@med.uoeh-u.ac.jp)
University of Occupational and Environmental Health Japan: Sangyo Ika Daigaku https://orcid.org/0000-0002-0807-7139

Research article

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Abstract

Objectives: Mepolizumab (MPZ), an anti-interleukin-5 antibody, is effective for treating eosinophilic granulomatosis with polyangiitis (EGPA). However, its effectiveness has not been adequately evaluated in real-world clinical practice. In this study, we assessed the effectiveness and safety of 300 mg MPZ for relapsing/refractory EGPA resistant to corticosteroids (CS) for 1 year in real-world settings.

Methods: We administered MPZ (300 mg) to 16 patients with relapsing/refractory EGPA resistant to CS (with-MPZ). We also retrospectively collected data from the same patients for 12 months before administering MPZ (without-MPZ). The primary endpoint was the 12-month remission rate after MPZ administration, and the secondary endpoints were the Birmingham vasculitis activity score (BVAS), vasculitis damage index (VDI), eosinophil count, changes in concomitant CS doses/concomitant immunosuppressant use, MPZ retention rate, and incidence of adverse events. The clinical course was compared between Without-MPZ and With MPZ.

Results: The 12-month remission rate after initiating MPZ was 75%. No change was observed in BVAS, eosinophil count, or concomitant CS dose in the without-MPZ, whereas all these parameters were significantly decreased in the with-MPZ. The number of patients on concomitant immunosuppressants also decreased in the with-MPZ. VDI did not increase in both groups. The MPZ retention rate was 100%, and only three patients (18.8%) had infections.

Conclusion: This study demonstrated that MPZ is effective and safe for EGPA, furthermore, compared to Without-MPZ, MPZ improves disease activity and possesses a higher remission rate and CS sparing effect.

Key Messages

MPZ is safe for the treatment of EGPA in real-world clinical practice.

Comparing to Without-MPZ, MPZ possesses the highly remission rate, and CS sparing effect.

Introduction

Eosinophilic granulomatosis with polyangiitis (EGPA) is a disease that is preceded by asthma or allergic rhinitis and causes various symptoms owing to vasculitis, including fever and purpura, and increases peripheral eosinophil counts.[1,2] Corticosteroids (CS) are used in remission induction therapy and maintenance therapy for EGPA. Patients with severe vasculitis symptoms and those poorly responding to CS are treated in combination with cyclophosphamide (CY), azathioprine (AZ), methotrexate (MTX), etc. Despite the standard of care, EGPA often relapses during CS dose reduction, and hence, CS dose reduction is often challenging.[3–5]

In recent years, mepolizumab (MPZ), an anti-interleukin-5 antibody, has been reported to extend the remission period of EGPA and reduce CS dose.[6] Although MPZ was listed in the National Health Insurance drug price list for treating EGPA in Japan in 2018, its effectiveness and safety have not been adequately evaluated in real-world clinical practice. While the dose of MPZ administered in previous studies was 100 mg/month, which is the same dose used for treating bronchial asthma, an MPZ dose of 300 mg is used in only a few countries, including Japan. Thus, we investigated the effectiveness and safety of MPZ at a dose of 300 mg/month in real-world settings.

Patients And Methods

Patients

In this study, MPZ (300 mg) was administered to 16 patients with relapsing or refractory EGPA who were receiving the standard of care, mainly CS.[7,8] All patients were diagnosed with EGPA according to the diagnostic criteria for EGPA, as proposed by the Japanese Ministry of Health, Labour and Welfare, and also met the classification criteria of the American College of Rheumatology[9] (Table 1, Supplementary Table 1). Patients with remission, relapsing EGPA, and refractory EGPA were defined as follows according to the reference of the Mepolizumab Treatment in Relapsing or Refractory EGPA trial[6]: patients with remission were those who had a Birmingham vasculitis activity score (BVAS) of 0 and were treated with oral CS at a dose of ≤4 mg/day; patients with relapsing EGPA were those for whom the oral CS dose was increased, concomitant immunosuppressive therapy was started, concomitant immunosuppressant dose was increased, or BVAS was increased[10] or who had a history of hospitalisation; and patients with refractory EGPA were those who experienced no relapse and achieved no remission within the last 1 year.

The patients were followed for 12 months after the introduction of MPZ at our hospital and affiliated institutions, during the period between the domestic introduction of MPZ in May 2018 until August 2020 (with-MPZ). In addition, we retrospectively collected data of the same patients for 12 months before initiating MPZ therapy (without-MPZ). All patients received maintenance therapy according to the standard of care. The SoC in this study was defined as treatment with CS, intravenous cyclophosphamide (IV-CY), Intravenous immunoglobulin, azathioprine, Methotrexate (MTX), or cyclosporine (CsA)/tacrolimus (TAC). The Human Ethics Review Committee of our university reviewed and approved this study (No. H27-014). Also, we complied the Declaration of Helsinki. All participants provided informed consent prior to inclusion in the study. Details that might disclose the identity of study subjects were omitted.

Clinical measurement

We administered MPZ therapy at a dose of 300 mg/month to 16 patients with relapsing or refractory EGPA and evaluated its effectiveness and safety for a year. The primary endpoint was the remission rate. The secondary endpoints were BVASs for the overall and each item, vasculitis damage index (VDI) for the overall and each item,[11,12] eosinophil count, daily and cumulative concomitant CS doses, presence or absence of changes/addition of immunosuppressant(s), MPZ retention rate, and incidence of adverse events. In addition, the reduction in BVAS, change in VDI, reduction in peripheral eosinophil counts, and cumulative concomitant CS doses were compared between the 1-year period before initiating MPZ therapy (without-MPZ) (month −12 to month 0) and the 1-year period after initiating MPZ (with-MPZ) (month 0 to month 12). To express the results of the two groups synchronously, the original timeframes of the without-MPZ [−12 (baseline), −11, −9, and −6 months) were represented as 0 (baseline), 1, 3, and 6 months, respectively.

Statistical analysis

The data are expressed as median (interquartile range). For statistical analysis, data from cases in which MPZ was discontinued, or relapsed were complemented using the last observation carried forward method. Differences between the groups (with-MPZ vs. without-MPZ), and between baseline data and those measured at each observation point) (with MPZ: month 0 vs. month 1, 3, 6, 12) were compared using Fisher's exact test and Wilcoxon sum rank test.

The timeframes of the two groups were represented synchronously and compared [−12 months (baseline) of the without-MPZ corresponded to 0 months (baseline) of the with-MPZ]. All reported *P* values were 2-sided. In addition, remission was defined as a BVAS 0 and CS less than 4mg/day. All analyses were computed by using JMP version 14.0.0 (SAS Institute Inc).

Results

Patient background

The characteristics of the patients are shown in Table 1. The characteristics of each patient at the diagnosis of EGPA are shown in Supplementary Table 1. At the time of initiating MPZ therapy, the median age [interquartile range] of the 16 patients with EGPA was 61.5 [53.3–70.5] years, and the disease duration was 54 [22–144] months. Regarding medical history, all patients were treated with CS. The without-MPZ included four patients with relapsing EGPA, 11 with refractory EGPA, and one with remission, while the with-MPZ included 10 patients with relapsing EGPA and six with refractory EGPA. No statistically significant differences were observed in the concomitant CS dose or the rate of concomitant immunosuppressant use between both groups. There were also no statistically significant differences in BVAS, VDI, positivity rate for anti-neutrophil cytoplasmic antibody, eosinophil count, or C-reactive protein level between the two groups.

Effectiveness of MPZ

The remission rates at 1 year (the primary endpoint) were 6.3% at month 1, 12.5% (1/16 patients) at month 3, 6.3% at month 6, and 0% at month 12 in the without-MPZ, thereby showing no statistically significant differences. The corresponding rates in the with-MPZ were 12.5% at month 1, 31.3% at month 3, 50.0% at month 6, and 75.0% at month 12. In this group, the remission rate significantly increased at month 3 onwards (Figure 1A). The remission rate at 1 year was significantly higher in the with-MPZ than in the without-MPZ.

In the without-MPZ, BVASs were 0 [0–2.0] at month 1, 0 [0–2.0] at month 3, 0 [0–2.0] at month 6, and 1.0 [0–3.8] at month 12, showing no significant change from the BVAS at month 0. In the with-MPZ, BVASs were 0 [0–2.8] at month 1, 0 [0–0] at month 3, 0 [0–0] at month 6, and 0 [0–0] at month 12. BVASs at month 1 and afterward significantly decreased from BVAS at month 0 (Figure 1B). The decrease in BVAS during the 1-year period in the with-MPZ was 0.5 [0–3.5], which was significantly larger than −2.0 [−3.0–0] in the without-MPZ (Figure 2A).

Based on the changes in BVASs for each item, respiratory symptoms were exacerbated in the without-MPZ but improved immediately after initiating MPZ therapy. The number of patients with symptoms decreased from 11/16 to 2/16 after 1 year of treatment. Ear, nose, and throat symptoms also improved as the number of patients with symptoms decreased from 3/16 to 6/16 patients at 1 year after initiating MPZ therapy. In contrast, neuropathy did not improve in either the with-MPZ or without-MPZ. In the with-MPZ, no organ dysfunction was exacerbated at month 12 (Table 2).

In the without-MPZ, VDI scores were 3.5 [3.0–4.8] at month 1, 4.0 [3.0–5.5] at month 3, 4.0 [3.0–5.5] at month 6, and 4.0 [3.0–5.5] at month 12, showing no significant increase compared with those at month 0. In the with-MPZ, VDI scores were 4.0 [3.0–5.5] at month 1, 4.0 [3.0–5.5] at month 3, 4.0 [3.0–5.5] at month 6, and 4.0 [3.0–5.5] at month 12, showing no significant changes (Figure 1C). The increase in the VDI score during the 1-year period was 0 [0–0.8] in the without-MPZ and 0 [0–0] in the with-MPZ, showing no significant difference between the two groups (Figure 2B).

In the without-MPZ, eosinophil counts were 280.4 [63.2–426.8]/μL at month 1, 217.8 [93.3–1354.2]/μL at month 3, and 293.9 [39.1–880.7]/μL at month 6, showing no significant changes compared with those at month 0. In the with-MPZ, eosinophil counts were 54.8 [10.6–99.8]/μL at month 1, 25.2 [12.8–53.9]/μL at month 3, 29.4 [9.63–42.5]/μL at month 6, and 28.8 [20.5–68.0] at month 12, showing significant reduction at month 1 onwards (Figure 1D). The reduction in the eosinophil count during the 1-year period in the with-MPZ was 146.2 [9.88–2449.9], which was significantly higher than −8.8 [−2927.4–175.4] in the without-MPZ (Figure 2C).

In the without-MPZ, concomitant CS doses were 8.0 [5.0–10.0] mg/day at month 1, 7.0 [3.5–10.0] mg/day at month 3, 6.5 [2.6–10.0] mg/day at month 6, and 6.0 [2.6–10.0] mg/day at month 12, showing no significant changes compared with those at month 0. In the with-MPZ, concomitant CS doses were 6.5 [2.6–10.0] mg/day at month 1, 5.0 [2.3–7.4]

mg/day at month 3, 4.5 [0.5–5.0] mg/day at month 6, and 2.5 [0.1–3.8] mg/day at month 12, showing significant reduction at month 3 onwards (Figure 1E). When cumulative concomitant CS doses were compared between the with-MPZ and without-MPZs, the doses were 2665 [1473.8–3993.8] mg/year in the without-MPZ and 1655 [570.0–2190.0] mg/year in the with-MPZ. The cumulative concomitant CS doses significantly decreased in the with-MPZ (Figure 2D). The changes in the use of immunosuppressant(s) are shown in Table 3. The number of patients with concomitant immunosuppressant(s) use reduced from 10 to nine patients at 1 year in the without-MPZ and from nine to five patients in the with-MPZ.

MPZ retention rate and safety

The 1-year MPZ retention rate was 100%. Although three patients had an infection, all patients continued MPZ. Adverse events before and after initiating MPZ therapy are shown in Table 4. All three patients who had an infection after initiating MPZ therapy had the same infection within 1 year before initiating MPZ therapy. No patients had a new infection after initiating therapy.

Discussion

This study demonstrated the effectiveness and safety of MPZ for relapsing or refractory EGPA in a real-world setting by comparing the clinical courses before and after initiating MPZ therapy. During the 1-year period before initiating MPZ therapy, BVASs increased as CS doses were tapered, and the effect of immunosuppressants in controlling disease activity was inadequate to allow CS dose reduction. While many patients used AZ as a concomitant immunosuppressant before initiating MPZ therapy in this study, it has been previously reported that AZ is not useful for maintenance therapy.[13] In this study, BVASs and eosinophil counts significantly decreased at 1 month after initiating MPZ therapy. The doses of CS and immunosuppressants were also successfully reduced (Figs. 2A, C, and D). MPZ was a useful drug for maintenance therapy that could exert a more consistent effect on controlling disease activity than existing immunosuppressants.

The MPZ retention rate was 100%, and the incidence of infections tended to reduce (Table 2). These findings confirmed the safety of MPZ. In particular, severe infection requiring hospitalisation was noted only in two patients with a history of infection, and there was no incidence of new serious infection. These results can be considered very useful. The reduced incidence of infection might be attributable to the significant reduction in concomitant CS doses and the reduced number of patients with concomitant immunosuppressant use after initiating MPZ therapy (Fig. 2D, Table 4). Long-term oral administration of CS induces infections and various complications, including osteoporosis, diabetes, hypertension, dyslipidaemia, and femoral head necrosis. We showed neither a significant increase in VDI scores nor an increased incidence of complications owing to CS after initiating MPZ therapy. Thus, we demonstrated that MPZ therapy was sufficiently effective in controlling disease activity and could prevent adverse events induced by CS and immunosuppressants. In the future, it is important to investigate for a long period whether long-term MPZ therapy allows dose reduction or disretention of CS without relapse and whether VDI increases.

There are only a few countries where subcutaneous MPZ injection at a dose of 300 mg for EGPA has been listed in the National Health Insurance drug price list, as in Japan. Although there are a few case reports of the use of MPZ at a dose of 300 mg[14] and a case series of the use of MPZ at 100 mg for treating comorbid asthma,[15] no studies have investigated the safety and effectiveness of MPZ at 300 mg in real-world clinical practice. This is the strength of this study. However, this study had a few limitations. Our sample size was small, and we compared parameters in the same set of patients. However, we consider that this is the first study demonstrating the safety and effectiveness of MPZ at 300 mg in the real-world setting.

In the future, studies with larger sample sizes and longer follow-up periods are needed to assess the long-term effectiveness of MPZ in controlling disease activity. Many previous reports describe the use of MPZ in treating asthma, and asthma activity has been evaluated using pulmonary function test and the Asthma Control Questionnaire (ACQ-5). However, because this study aimed to assess vasculitis, disease activity was mainly assessed using BVAS. There were also some patients without results of pulmonary function test or ACQ-5. Hence, these tests were not included in the endpoints.

In conclusion, this study demonstrated that MPZ therapy at a dose of 300 mg in patients with relapsing or refractory EGPA could reduce doses of CS and immunosuppressants without any exacerbation of organ dysfunctions and could lead to remission.

List Of Abbreviations

MPZ: Mepolizumab

EGPA: Eosinophilic granulomatosis with polyangiitis

CS: Corticosteroids

BVAS: Birmingham vasculitis activity score

VDI: vasculitis damage index

CY: cyclophosphamide (CY)

IV-CY: intravenous cyclophosphamide

AZ: azathioprine

MTX: methotrexate

CsA: cyclosporine

TAC: tacrolimus

without-MPZ: 1-year period before initiating MPZ therapy

with-MPZ: 1-year period after initiating MPZ

ACQ-5: Asthma Control Questionnaire

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from the University of Occupational and Environmental Health, Japan Ethics Committee following the Helsinki declaration. This retrospective study was approved by the institutional review board, and the requirement to obtain informed consent was waived.

Consent for publication

Not applicable.

Availability of data and materials

Not applicable.

Competing interest

Y. Tanaka, has received speaking fees and/or honoraria from Daiichi-Sankyo, Astellas, Eli Lilly, Chugai, Sanofi, Abbvie, Pfizer, YL Biologics, Bristol-Myers, Glaxo-Smithkline, UCB, Mitsubishi-Tanabe, Novartis, Eisai, Takeda, Janssen, Asahi-kasei and has received research grants from Mitsubishi-Tanabe, Bristol-Myers, Eisai, Chugai, Takeda, Abbvie, Astellas, Daiichi-Sankyo, Ono, MSD, Taisho-Toyama.

K. Nakano, has received speaking fees from Astellas, UCB, Mitsubishi-Tanabe, Eisai and has received research grants from Mitsubishi-Tanabe, Eisai, and Eli Lilly.

S. Nakayamada received speaking fees and/or honoraria from Bristol-Myers, Sanofi, Abbvie, Eisai, Eli Lilly, Chugai, Asahi-kasei and Pfizer (less than $10,000 each), and also research grants from Mitsubishi-Tanabe, Takeda, Novartis and MSD.

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Author's contributions: MU contributed to the study design, overall review, writing of the manuscript, and the other authors were involved in the performance of the study and review of the manuscript. YT, MI, KN, SI, SN, participated in the study design and coordination. All authors read and approved the final manuscript.

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Tables

Table 1
Baseline characteristic of 16 Patients with Eosinophilic Granulomatosis with Polyangiitis

	without MPZ(n = 16)	with MPZ(n = 16)	p value*
Clinical manifestations at diagnosis, n (%)	Asthma 16 (100), General 10 (62.5), Cutaneous 8 (50.0), ENT 5 (31.3), Chest 8 (50.0), Cardiomyopathy 3 (18.8), Abdominal 1 (6.3), Neuropathy 8 (50.0), ANCA positive status 5 (31.3), Biopsy findings 12 (75)		
Male/Female/age at MPZ introduction	7/9/61.5[53.3–70.5]		
Disease duration (Months) at MPZ introduction	54[22–144]		
Treatment history, n (%)	CS pulse 1 (6.3), High-dose CS 14 (87.5), low-dose CS 2 (12.5), IVCY 9 (56.3), IVIG 6 (37.5), RTX 1 (6.3), MTX 6 (37.5), AZ 12 (75.0), TAC 1 (6.3)		
Relapsing/Refractory/Remission, n (%)	4 (25.0)/11 (68.7)/1 (6.3)	10 (62.5) / 6 (37.5)/ 0 (0)	
Concomitant CS dose (PSL mg/day)	8.0[5.0–10.0]	6.5 [2.6–10.0]	0.0742
Concomitant CS < 4 mg/day (PSL), n (%)	3 (18.8)	5 (31.3)	0.6851
Concomitant immunosuppresant, n (%)	AZ 6 (37.5), MTX 5 (31.3), TAC 1 (6.3)	AZ 6 (37.5), MTX 4 (25.0), TAC 1 (6.3)	1.0000
without immunosuppressant, n (%)	6 (37.5)	7 (43.8)	
BVAS	0 [0–2.0]	1.0 [0-3.8]	0.1138
BVAS > 0, n (%)	4 (25.0)	8 (50.0)	0.2734
BVAS items	Asthma 2 (12.5), Sinonasal 2 (12.5), Chest 1 (6.3)	Asthma 6 (37.5), General 1 (6.3), Cutaneous 2 (12.5), Sinonasal 2 (12.5), Chest 3 (18.8),	
VDI	3.5 [3.0-4.8]	4.0 [3.0-5.5]	0.6380

CS: corticosteroid (prednisolone or equivalent), IVCY: cyclophosphamide pulse therapy i.v., RTX: Rituximab, MTX: methotrexate, AZ: azathioprine, TAC: tacrolimus, BVAS; Birmingham Vasculitis Activity Score, VDI; Vasculitis damage index, Data are shown by median[quartile] or n (%). *P* values were determined by Fisher's exact test or Wilcoxon rank sum test. p*<0.05: without MPZ group (n = 16) vs. with MPZ group (n = 16)

	without MPZ(n = 16)	with MPZ(n = 16)	p value*
VDI items	Chronic bronchial asthma 16 (100), Chronic respiratory failure 1 (6.3), Abnormal respiratory function 7 (43.8), Old myocardial infarction 2 (12.5), Cardiomyopathy 2 (12.5), Low vision 1 (6.3), Chronic sinusitis 6 (37.5), Deafness 3 (18.8), Peripheral neuropathy 8 (50.0), Diabetes 4 (25), Hypertension 4 (25), Osteoporosis 5 (31.3)， Other 3 (18.8)	Chronic bronchial asthma 16 (100), Chronic respiratory failure 1 (6.3), Abnormal respiratory function 8 (50.0), Old myocardial infarction 2 (12.5), Cardiomyopathy 2 (12.5), Low vision 1 (6.3), Chronic sinusitis 7 (43.8), Deafness 3 (18.8), Peripheral neuropathy 8 (50.0), Diabetes 4 (25), Hypertension 4 (25), Osteoporosis 5 (31.3)， Other 5 (31.3)	
ANCA positive status, n (%)	0 (0)	1 (6.3)	1.0000
Absolute eosinophil count (/μL)	303.6 [55.2-482.6]	183 [60.0-2479]	0.3757
CRP (mg/dL)	0.06 [0.03–0.09]	0.09 [0.05–0.24]	0.0593

CS: corticosteroid (prednisolone or equivalent), IVCY: cyclophosphamide pulse therapy i.v., RTX: Rituximab, MTX: methotrexate, AZ: azathioprine, TAC: tacrolimus, BVAS; Birmingham Vasculitis Activity Score, VDI; Vasculitis damage index, Data are shown by median[quartile] or n (%). *P* values were determined by Fisher's exact test or Wilcoxon rank sum test. p*<0.05: without MPZ group (n = 16) vs. with MPZ group (n = 16)

Table 2
Changes in organ damage before and after the introduction of Mepolizumab

	Without MPZ				With MPZ				
	-12M	-11M	-9M	-6M	0M	1M	3M	6M	12M
General symptoms	0	0	1 (6.3%)	1 (6.3%)	1 (6.3%)	1 (6.3%)	0	1 (6.3%)	0
Cutaneous manifestations	1 (6.3%)	1 (6.3%)	1 (6.3%)	1 (6.3%)	2 (12.5%)	2 (12.5%)	0	1 (6.3%)	0
ENT manifestations	6 (37.5%)	6 (37.5%)	6 (37.5%)	6 (37.5%)	6 (37.5%)	6 (37.5%)	6 (37.5%)	4 (25.0%)	3 (18.8%)
Chest manifestations	6 (37.5%)	6 (37.5%)	8 (50.0%)	8 (50.0%)	11 (68.8%)	5 (31.3%)	2 (12.5%)	2 (12.5%)	2 (12.5%)
Nervous system manifestations	7 (45.8%)	7 (45.8%)	7 (45.8%)	8 (50.0%)	8 (50.0%)	8 (50.0%)	7 (43.8%)	7 (43.8%)	7 (43.8%)

ENT; Ear, Nose, Throat. Mepolizumab; MPZ

Table 3
Changes in the Concomitant immunosuppressants use before and after the introduction of Mepolizumab

	Without MPZ				With MPZ				
Case No	-12M	-11M	-9M	-6M	0M	1M	3M	6M	12M
1	MTX 8 mg	MTX 8 mg	none	none	none	none	none	none	none
2	MTX 8 mg +AZ 125 mg	MTX 8 mg +AZ 125 mg	MTX 8 mg +AZ 125 mg	MTX 8 mg +AZ 125 mg	MTX 8 mg +AZ 125 mg	AZ125mg	AZ125mg	AZ125mg	AZ100mg
3	AZ50mg	AZ50mg	AZ 50 mg	AZ 50 mg	AZ 50 mg	AZ 50 mg	AZ 50 mg	AZ 50 mg	AZ 50 mg
4	none	none	AZ 50 mg	none	none	none	none	MTX 8 mg	MTX 8 mg
5	MTX 6 mg +AZ 50 mg	MTX 6 mg +AZ 50 mg	MTX 6 mg +AZ 50 mg	MTX 6 mg +AZ 50 mg	MTX 6 mg +AZ 50 mg	AZ 50 mg	AZ 50 mg	AZ 50 mg	AZ 50 mg
6	MTX 16 mg	MTX 16 mg	MTX 16 mg	MTX 16 mg	MTX 16 mg	MTX 16 mg	MTX 10 mg	MTX 4 mg	none
7	none	none	none	none	none	none	none	none	none
8	MTX 12 mg	MTX 12 mg	MTX 12 mg	MTX 12 mg	MTX 12 mg	none	none	none	none
9	AZ 50 mg	AZ 50 mg	AZ 50 mg	AZ 50 mg	AZ 50 mg	none	none	none	none
10	none	none	none	none	none	none	none	none	none
11	TAC 3 mg	TAC 3 mg	TAC 3 mg	TAC 3 mg	TAC 3 mg	none	none	none	none
12	none	none	none	none	none	none	none	none	none
13	AZ 50 mg	AZ 50 mg	AZ 50 mg	AZ 50 mg	AZ 50 mg	AZ 50 mg	AZ 50 mg	AZ 50 mg	AZ 50 mg
14	none	none	none	none	none	none	none	none	none
15	AZ 100 mg	AZ 100 mg	AZ 100 mg	AZ 100 mg	AZ 100 mg	none	none	none	none
16	none	none	none	none	none	none	none	none	none

IVCY: cyclophosphamide pulse therapy i.v., MTX: methotrexate, AZ: azathioprine, TAC: tacrolimus, MPZ: Mepolizumab

Table 4
Adverse events before and after introduction of Mepolizumab.

Case No.	without MPZ	With MPZ
1	Bacterial pneumonia(Hospitalization)	Bacterial pneumonia(Hospitalization)
2	none	none
3	none	none
4	Drug-induced liver injury	none
5	Sinusitis surgery□Bacterial bronchitis	none
6	Bacterial bronchitis□Infectious otitis media	none
7	none	none
8	none	none
9	none	none
10	none	none
11	Bacterial pneumonia(Hospitalization)	Bacterial pneumonia(Hospitalization)
12	none	none
13	Bacterial pneumonia(Hospitalization)	none
14	Bacterial bronchitis	none
15	Bacterial pneumonia	Bacterial pneumonia
16	none	none
Mepolizumab: MPZ		

Figures

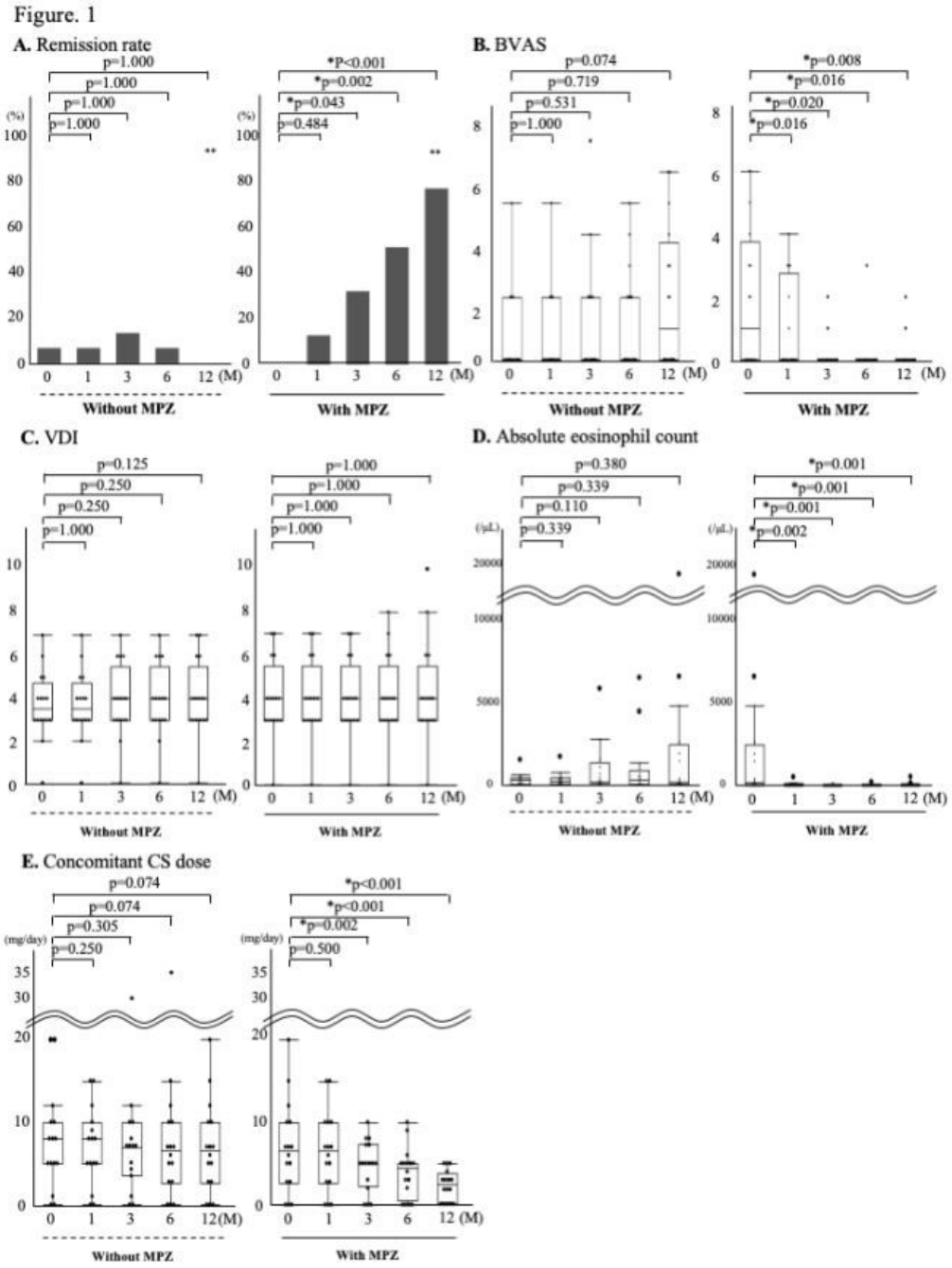

Figure 1

Comparison of effectiveness between the Without-MPZ and the With-MPZ. (A) Remission rates. (B) BVAS. (C) VDI. (D) Eosinophil counts. (E) Concomitant CS doses. Abbreviations: BVAS: Birmingham vasculitis activity score, CS: corticosteroid, VDI; vasculitis damage index P values were determined by Fisher's exact test or Wilcoxon rank sum test. p*<0.05: baseline (month 0) vs. each observation points (month 0,1, 3, 6 and 12).

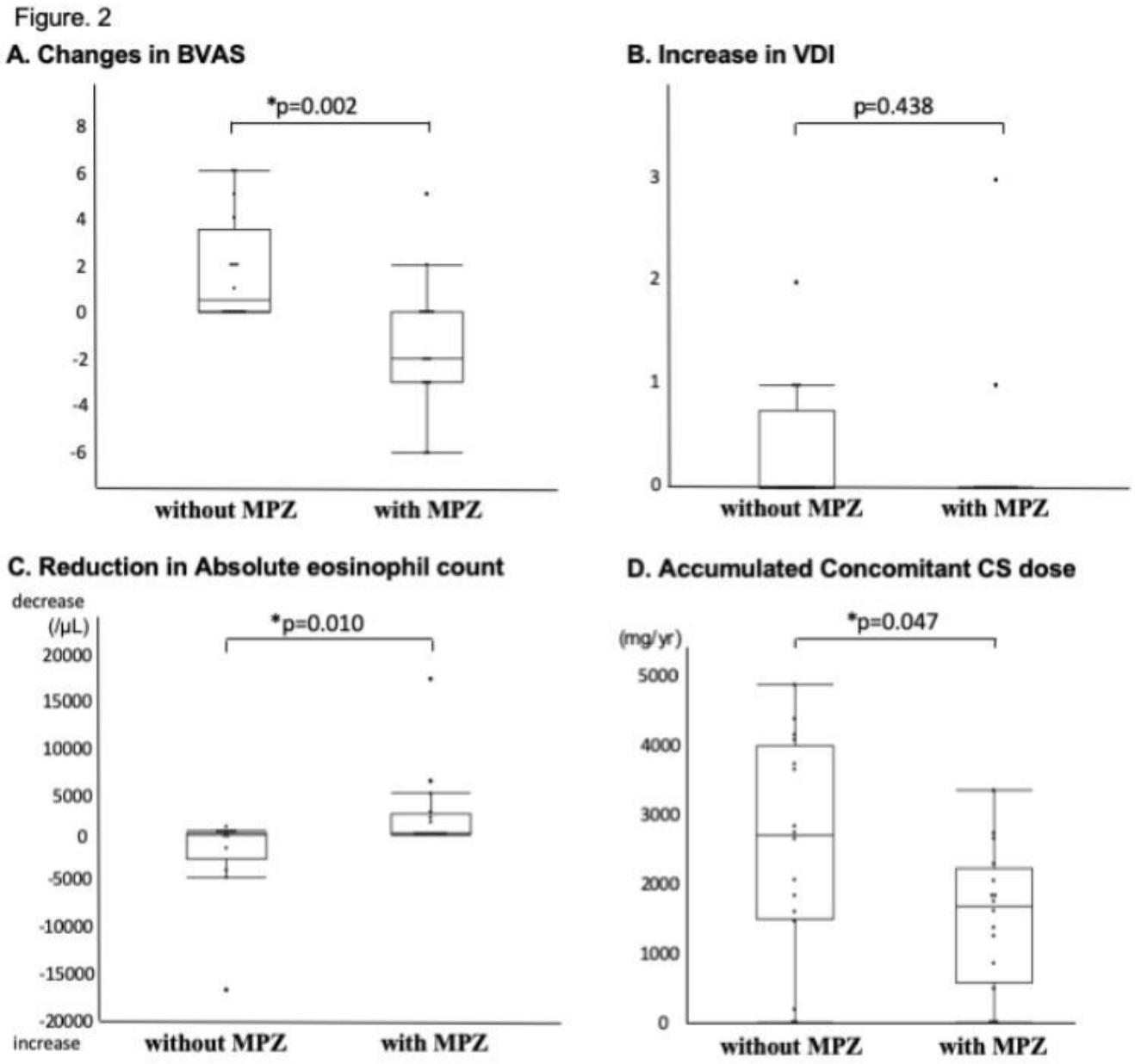

Figure 2

Comparison of changes of each item between the 12-months period in Without-MPZ and with-MPZ. (A) changes in BVAS, (B) increase in VDI, (C) reduction in peripheral eosinophil counts (/ul), and (D) accumulated concomitant CS dose (mg/year) Abbreviations: BVAS: Birmingham vasculitis activity score, CS: corticosteroid, VDI; vasculitis damage index P values were determined by Wilcoxon rank sum test. p*<0.05: Without-MPZ vs. With-MPZ.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- MPZSupplementaryTable1.docx