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Treatment patterns of patients with multiple sclerosis in Guangzhou, China

[1]Rui Li, [1]Jingqi Wang, [1]Jing Li, [1]Yuge Wang, [1]Haotian Wu, [1]Ping Fan, [2]Alexander Y. Lau, [1,2,3,4]Allan G. Kermode, [1]Wei Qiu

[1]Department of Neurology, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; [2]Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Shatin, China; [3]Centre for Neuromuscular and Neurological Disorders, University of Western Australia, Perth, WA; [4]Department of Neurology, Sir Charles Gairdner Hospital, Queen Elizabeth II Medical Centre, Perth, WA; [5]Institute of Immunology and Infectious Diseases, Murdoch University, Perth, WA, Australia

Abstract

Background & Objective: Disease-modifying treatments (DMTs) for multiple sclerosis (MS) are widely used in Western countries. In China, however, the current treatment patterns of MS patients are not well characterized. This is to explore the gap between the current treatments in Guangzhou, Southern China and those given in Western countries. *Methods:* We performed a survey of MS patients at department of neurology, a tertiary MS referral centre in Guangzhou, concerning treatments of MS in Southern China. The clinical data in patients were collected. The initial treatment, drug withdrawal or switching profile, and therapeutic effect of existing treatments in MS patients were analyzed. *Results:* The ratio of MS patients who receive DMTs in Guangzhou China is extremely low. Among the 178 patients studied, only 28.09% received initial treatment with DMTs. MS patients who receive initial treatment with first-line DMTs have higher drug withdrawal rates (32.6%) and drug switching rates (30.43%) than those of western populations. The main reasons for withdrawal of first-line DMTs were doctor's advice (maintenance of remission) (40.00%), economic burden(20.00%), and no channels to buy drugs(13.33%). In MS patients initially treated with first-line DMTs who switched to other drugs, a gap between treatments was common (8/14; 57.14%). There were 18 patients with highly active MS receiving treatment with rituximab. Annual relapse rate after treatment significantly decreased than that before treatment (0.74 vs. 1.50 , $P < 0.001$). *Conclusions:* DMTs for MS in Guangzhou, Southern China appear to lag behind those in Western countries. Much work is needed to improve drug accessibility and affordability of DMTs in China. Rituximab is an option for highly active MS in limited medical-resource countries.

Keywords: Multiple sclerosis, disease-modifying treatment, Guangzhou, China

INTRODUCTION

Multiple sclerosis (MS) is a chronic demyelinating disease of the central nervous system characterized by inflammation and neurodegeneration. MS causes troublesome or disabling physical symptoms involving mobility, vision, coordination, cognitive dysfunction, fatigue, and pain. Sufferers' quality-of-life may be further reduced by mood disorders and limitations in employment and social functioning.[1] Although there is no cure for MS, a few disease-modifying treatments (DMTs) are available to help patients experience less frequent relapses and slow progression of the disease. First-generation DMTs [interferon (IFN)-β, and glatiramer acetate] became available in the 1990s. Over the past decade, treatment options have expanded with the introduction of new therapies, such as natalizumab, fingolimod, teriflunomide, dimethyl fumarate (DMF), alemtuzumab, cladribine, and ocrelizumab.[2,3]

Treatment of MS patients with DMTs is well characterized and widely used in Western countries where the incidence and prevalence of the disease is relatively high (>100/100,000).[4] Because the incidence of MS is relatively low in China (0-5/100,000)[4], numbers of DMTs on the market and funded status for MS in China have lagged behind those in Western countries. There are more than ten DMTs for MS approved by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), while the only drugs on the market are interferon

Address correspondence to: Wei Qiu, Multiple Sclerosis Center, Department of Neurology, The Third Affiliated Hospital of Sun Yat-Sen University, No. 600 Tianhe Road, Guangzhou, Guangdong Province 510630, China. Tel: +86 20 87516822, E-mail: qiuwei120@vip.163.com

(Betaferon) and teriflunomide (Aubagio) in China. Recently, fingolimod (Gilenya) has been approved by China Food and Drug Administration (CFDA). Because of the high price of DMTs, they are financed by the government in many Western countries. In China, only teriflunomide has just been approved for national health insurance. Traditional immunosuppressants are an alternative treatment for MS patients in China, because they are cheap and are effective for some MS patients, although they are not approved to treat MS patients by FDA.

The current treatment patterns of MS in China is not well known. Previous studies only provided some epidemiological data on MS in China.[5,6] This study reviews for the first time the current patterns of treatment in Chinese patients with MS by reporting the clinical experience of a single Center, which is the largest referral center for MS in Southern China, and aims to explore the gap between the current treatments of MS in Guangzhou, Southern China and that in western countries. It is important for understanding potential opportunities to improve care for MS patients in China.

METHODS

Clinical data collection

During the period from December 2017 to March 2019, a survey was conducted by neurologists at department of neurology, a tertiary MS referral centre in Guangzhou, to identify and investigate all outpatients with MS who were able to be followed-up to the present time. Patients were included in the study if they fulfilled the inclusion criteria for MS.[7] The following data on patients were retrieved: age, gender, disease course, diagnosis, first hospital visit, initial treatment, channels available for purchasing drugs, drug withdrawal, drug switching, reasons for drug withdrawal or switching, relapses, and the Expanded Disability Status Scale (EDSS). Disease onset was defined as the first clinical attack. Corticosteroids treatment was defined as ongoing oral low-dose corticosteroids (10-20mg per day). In our study, first-line DMTs included IFN-β, teriflunomide and DMF. Second-line DMTs included fingolimod and mitoxantrone. All patients gave their written informed consent to participate in this study, which was approved by the Ethics Committee of the Third Affiliated Hospital of Sun Yat-sen University (2007-33).

Analysis

The continuous variables were described as median (upper quartile, lower quartile), because these data were not normally distributed. Differences between groups of patients according to their treatments were assessed using Mann-Whitney U test, Kruskal-Wallis H test for quantitative variables, and the chi-squared test for categorical variables. Kaplan-Meier survival analysis was performed to determine time-dependent outcomes, and differences between survival curves were analyzed using the log-rank test. *P*-values <0.05 were considered statistically significant. Statistical analysis was performed using SPSS® version 16.0 (Microsoft Corporation, San Francisco CA).

RESULTS

Initial treatment profiles of MS patients at our center

One hundred and seventy-eight patients who were able to be followed-up were identified at our center, including 118 females and 60 males. The average age at disease onset was 24 (range 20-32) years, and the average course of the disease was 12 months (range 1-43). The distribution of initial treatments for the patients in different years is shown in Figure 1. Before 2015, IFN-β, oral corticosteroids, and immunosuppressive agents were the main initial treatments given for MS. From 2016 to 2017, oral corticosteroids and immunosuppressants were still the main initial treatments, but since 2018 teriflunomide and immunosuppressive agents have become the main initial treatments for patients with MS.

The demographic and clinical characteristics of MS patients treated with DMTs or non-DMTs at our center are shown in Table 1. Among the 178 patients studied, 50 (28.09%) received initial treatment with DMTs (29 with IFN-β, 15 with teriflunomide, 2 with DMF, 3 with mitoxantrone, and 1 with fingolimod,), 97 patients (54.49%) received initial treatment with non-DMTs [91 with immunosuppressive agents or corticosteroids (21 with azathioprine, 7 with mycophenolate mofetil, 5 with methotrexate, 7 with tacrolimus, 51 with corticosteroids), and 6 with rituximab], and 31 patients (17.42%) received no therapy. At the last follow-up, only 18 of the 50 patients (36.00%) who initially received DMTs were still continuing this treatment, but 16 (32.00%) had discontinued DMTs, and 16 (32.00%) patients had switched to other drugs. Drug withdrawal and switching profile of different DMTs was

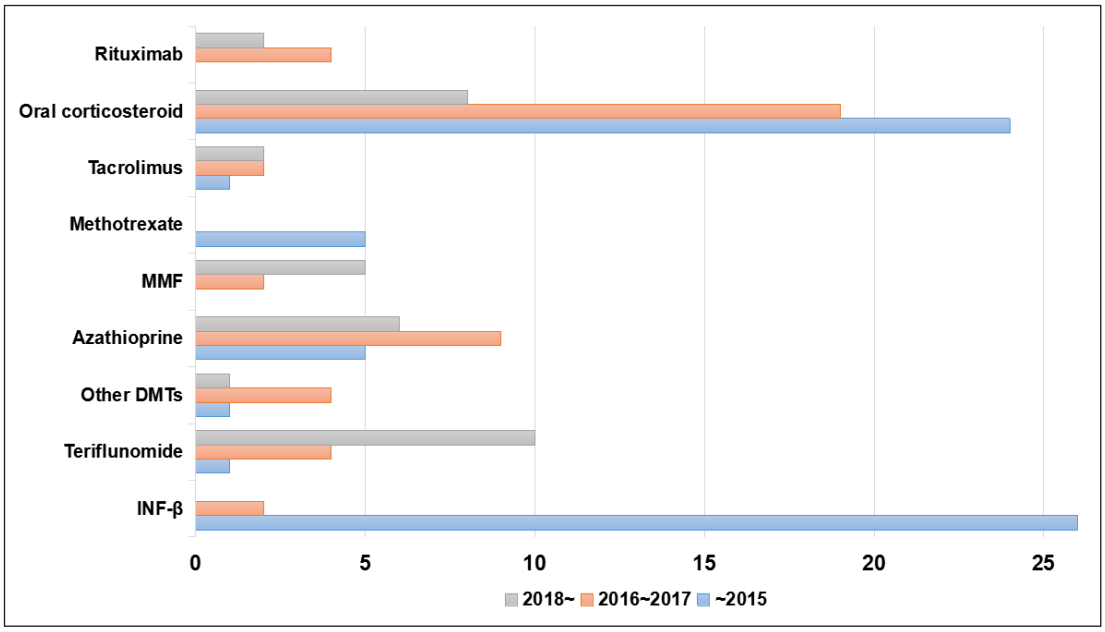

Figure 1: Distribution of initial treatment drugs for MS patients in different years. MS, multiple sclerosis, MMF, mycophenolate mofetil; Other DMTs: dimethyl fumarate, mitoxantrone, and fingolimod, IFN-β, interferon-β; DMTs, disease-modifying treatments.

shown in Figure 2. The main DMTs used by MS patients in Guangzhou, Southern China are IFN-β and teriflunomide. The drug withdrawal and switching rate of IFN-β was 14/29 (48.28%) and 12/29 (41.38%), while drug withdrawal and switching rate of teriflunomide was 1/15 (6.67%) and 1/15 (6.67%).

Drug withdrawals and drug switching after initial treatment with first-line DMTs or non-DMTs

Drug withdrawals and drug switching among patients initially treated with first-line DMTs are shown in Table 2. Of the 46 MS patients who were initially treated with first-line DMTs, 17 (36.96%) were continuing on this treatment at the last follow-

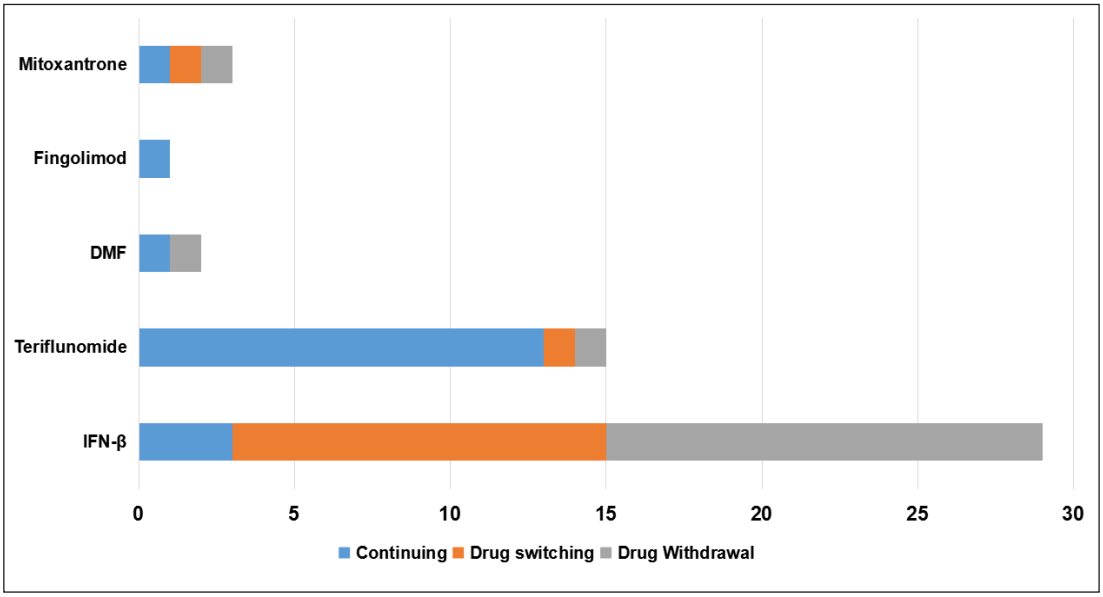

Figure 2. Drug withdrawal and switching profile of different DMTs. DMTs, disease-modifying treatments, IFN-β, interferon-β; DMF, dimethyl fumarate.

Table 1: Demographic and clinical characteristics of the MS patients

	DMTs (n = 50)			Non-DMTs (n = 97)					
	Total (n= 50)	First-line (n = 46)	2nd line (n = 4)	Total (n = 97)	Corticosteroid or immunosupressive agents (n = 91)	Rituximab (n = 6)	No treatment (n = 31)	*p**	*p***
Age, years	23.00 (17.50, 29.25)	22.00 (16.00, 28.25)	30.00 (25.00, 38.00)	24.00 (20.00, 32.00)	24.00 (20.00, 32.00)	20.00 (11.75, 26.50)	27.00 (20.00, 37.00)	0.225	0.551
Sex ratio (F:M)	33:17	31:15	2:2	65:33	63:29	2:4	21:10	NA	NA
Time from onset to treatment (months)	12.00 (2.00, 50.50)	7.00 (1.50, 47.50)	66.00 (41.50, 112.25)	11.50 (1.00, 37.75)	12.00 (1.00, 38.00)	11.00 (5.50, 36.00)	NA	NA	0.244
EDSS at onset	2.00 (1.00, 3.00)	2.00 (1.00, 3.00)	2.00 (1.25, 2.75)	2.00 (1.00, 3.00)	2.00 (1.00, 3.00)	5.00 (1.75, 6.13)	2.50 (1.50, 3.00)	0.205	0.194
EDSS at initial treatment	2.50 (1.25, 3.00)	2.00 (1.00, 3.00)	2.25 (2.00, 3.75)	3.00 (1.50, 4.00)	3.00 (1.50, 4.00)	2.00 (1.50, 3.25)	NA	NA	0.148
Follow-up EDSS	1.00 (0.50, 2.75)	1.00 (0.00, 2.00)	6.00 (3.63, 6.50)	1.50 (1.00, 3.00)	1.50 (1.00,3.00)	0.50 (0.00, 3.63)	1.00 (0.00, 3.00)	0.392	0.536
p value(EDSS at initial treatment vs follow-up EDSS)	0.064	0.010	0.074	<0.001	<0.001	0.063	NA	NA	NA
ARR before treatment	1.00 (0.82, 1.66)	1.00 (0.92, 1.93)	0.69 (0.44, 1.31)	1.00 (0.86, 1.31)	1.00 (0.86, 1.15)	1.00 (0.91, 2.39)	NA	NA	0.502
ARR after treatment	0.30 (0.00, 0.72)	0.33 (0.00, 0.72)	0.15 (0.00, 1.87)	0.18 (0.00, 0.71)	0.20 (0.00, 0.71)	0.00 (0.00, 0.50)	NA	NA	0.413
p value (ARR before treatment vs ARR after treatment)	<0.001	<0.001	0.146	<0.001	<0.001	0.022	NA	NA	NA
Follow-up after treatment (months)	52.00 (15.50, 67.50)	54.00 (14.50, 69.50)	28.50 (20.75, 38.50)	31.00 (15.25, 52.00)	33.00 (16.00, 52.00)	20.00 (9.50, 21.50)	NA	NA	0.168
Continuing treatment [n (%)]	18 (36.00)	17 (36.96)	1 (25.00)	45 (46.39)	39 (42.86)	6 (100.00)	NA	NA	0.228
Drug switching [n (%)]	16 (32.00)	14 (30.43)	2 (50.00)	36 (39.18)	36 (39.56)	0	NA	NA	0.539
Drug withdrawal [n (%)]	16 (32.00)	15 (32.61)	1 (25.00)	16 (16.49)	16 (17.58)	0	NA	NA	0.031

Values are means ± SD, unless otherwise indicated.

**p*-value for comparisons among the total DMTs, total non-DMTs, and no treatment groups.

***p*-value for the total DMTs compared with the total non-DMTs group.

ARR, annualized relapse rate: DMT, disease-modifying treatment; EDSS, Expanded Disability Scale Score; F, female; M, male.

Table 2: Drug withdrawal and switching in patients treated with first-line DMTs

	Non-switchers (n = 32)			Switchers (n = 14)					*p**
	Total (n = 32)	Maintain (n = 17)	Withdrawal (n = 15)	Total (n = 14)	First-line DMTs (n = 2)	Immunosuppr-essive therapy (n = 3)	2nd-line DMTs (n = 1)	Rituximab (n = 8)	
Age, years	23.50 (20.25, 32.25)	23.00 (20.00, 34.50)	24.00 (21.00, 29.00)	18.00 (15.75, 22.25)	19.50	22.00 (18.50, 27.00)	15	18.00 (16.00, 21.00)	0.018
Sex ratio (F:M)	23:9	11:6	12:3	8:6	1:1	2:1	F	4:4	NA
Time from onset to treatment (months)	7.00 (1.00, 37.00)	4.00 (1.00, 12.50)	21.00 (1.00, 46.50)	11.00 (5.25, 66.75)	48.50	15.00 (11.00, 53.00)	63.00	7.00 (2.00, 33.5)	0.288
EDSS at onset	1.50 (1.00, 3.00)	2.00 (1.50, 3.00)	1.00 (1.00, 1.75)	2.75 (2.00, 3.50)	2.25	3.00 (2.50, 4.25)	1.00	2.75 (2.00, 4.00)	0.008
Follow-up EDSS	1.00 (0.00, 2.00)	1.00 (0.00, 2.00)	1.00 (0.50, 2.25)	2.00 (0.50, 2.50)	2.50	2.00 (1.00, 3.00)	0	2.00 (1.00, 2.00)	0.495
Follow-up after treatment (months)	36.00 (8.00, 61.50)	10.00 (4.00, 16.00)	61.00 (56.00, 78.00)	61.50 (45.00, 85.00)	56.00	73.00 (64.5, 94.5)	52.00	62.00 (21.00, 85.50)	0.050
Gap between treatments [n(%)]	0	0	NA	8 (57.14)	2 (100.00)	2 (66.67)	0	4 (50.00)	<0.001
Gapperiod (months)	NA	NA	NA	21.50 ± 19.16	29.50	27.00	NA	14.75 ± 11.44	NA

Values are means ± SD, unless otherwise indicated.
**p*-value for thetotal non-switcher group compared with the total switcher group.
ARR, annualized relapse rate; DMT, disease-modifying treatment; EDSS, Expanded Disability Scale Score; F, female; M, male; NA, not available.

up, 15 (32.61%) had discontinued the treatment, and 14 (30.43%) had switched to other drugs. The reasons for withdrawal of first-line DMTs were doctor's advice (maintenance of remission) in 6 of the 15 patients (40.00)%, economic burden in 3 (20.00%), no channels to buy drugs in 2 (13.33%) (IFN-β1a and IFN-β1b were withdrawn from the market in China in 2010 and 2015), unknown reasons in 2 (13.33%), inefficacy in 1 (6.67%), and adverse effects in 1 (6.67%) [Figure 3A]. The reasons for drug switching (n = 14) were inefficacy in 6 patients (42.86%), no channels to buy drugs in 4 (28.57%), economic burden (21.43%) and unknown reasons in 1 (7.14%) [Figure 3B]. In MS patients initially treated with first-line DMTs who switched to other drugs, a gap between treatments was common (8/14; 57.14%) [Table 2].

In our clinical experience, only a minority of Chinese MS patients with mild-to-moderate disease activity choose first-line DMTs; others choose corticosteroids or immunosuppressive agents instead. For highly active relapsing MS or progressive MS, only a minority of patients choose second-line DMTs, while other patients receive treatment with rituximab. A total of 97 patients with MS were initially treated with non-DMTs (91 with oral corticosteroids or immunosuppressive agents and 6 with rituximab). Drug withdrawals and drug switching in patients initially treated with non-DMTs (oral corticosteroids or immunosuppressive agents) are shown in Table 3. Because rituximab is mainly used in highly active relapsing MS or progressive MS, it is not included in Table 3. Among these patients, 39 were continuing on this treatment at the last follow-up, 16 had discontinued their treatment, and 36 had switched to other drugs. The reasons for withdrawal of non-DMTs were doctor's advice (maintenance of remission) in 13 of the 16 cases (81.25%), and unknown reasons in 3 (18.75%)[Figure 3C]. The reasons for drug switching were inefficacy in all 36 cases (100.00%)[Figure 3D]. A treatment between treatments was less common in MS patients initially treated with non-DMTs who switched to other drugs (3/36; 8.33%).

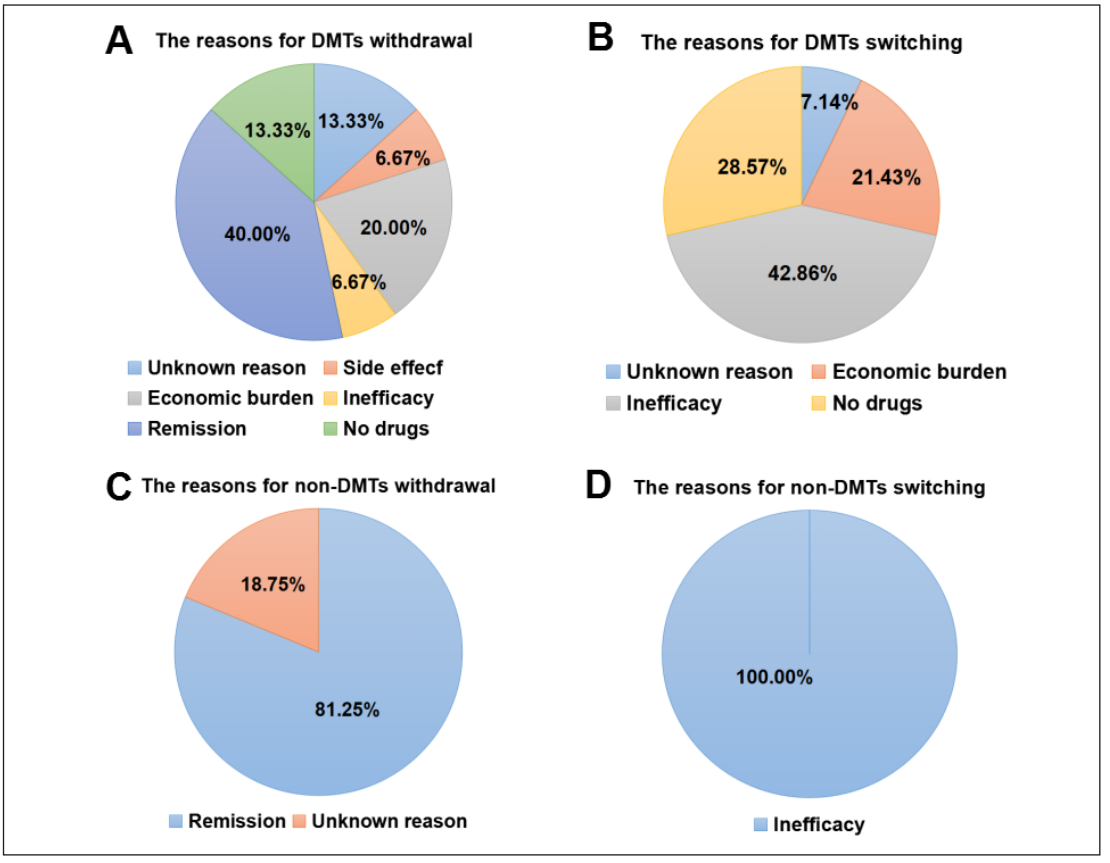

Figure 3. Reasons for drug withdrawal and switching in different groups of patients. DMTs, disease-modifying treatments.

Table 3: Drug withdrawal and switching in patients initially with non-DMTs (oral corticosteroids or immunosuppressive therapies)

	Non-switchers (n = 55)			Switchers (n = 36)					*p**
	Total (n = 55)	Maintain (n = 39)	Withdrawal (n = 16)	Total (n = 36)	First-line DMTs (n = 10)	Immunsuppressive therapy (n = 13)	2nd-line DMTs (n = 2)	Rituximab (n = 11)	
Age, years	25.00 (21.00, 32.00)	25.00 (21.50, 35.50)	26.00 (14.50, 31.00)	22.00 (18.50, 30.00)	28.50 (23.00, 36.00)	22.00 (20.00, 23.00)	44.00	18.00 (13.50, 21.00)	0.061
Sex ratio (F:M)	37:18	28:11	9:7	26:11	7:3	7:6	1:1	11:1	NA
Time from onset to treatment (months)	6.00 (1.00, 33.00)	12.00 (1.00, 37.50)	1.00 (1.00, 21.50)	12.00 (1.00, 43.00)	11.00 (1.00, 33.00)	8.00 (1.00, 14.00)	57.50	15.00 (1.00, 74.50)	0.775
EDSS at onset	2.00 (1.00, 3.00)	2.00 (1.00, 2.75)	2.00 (1.00, 3.00)	3.00 (1.25, 4.25)	1.50 (1.00, 3.00)	3.00 (2.00, 3.50)	4.75	3.00 (1.50, 5.00)	0.046
Follow-up EDSS	1.00 (1.00, 3.00)	1.00 (1.00, 3.00)	1.25 (0.50, 2.50)	2.00 (1.00, 3.00)	2.00 (1.00, 3.00)	1.00 (1.00, 3.00)	3.25	3.00 (1.25, 6.25)	0.043
Follow-up after treatment (months)	22.00 (10.50, 41.50)	15.00 (9.00, 41.50)	33.50 (20.00, 46.00)	43.50 (30.50, 58.50)	40.50 (29.00, 46.00)	40.00 (31.00, 52.00)	58.50	58.00 (32.00, 78.50)	<0.001
Gap between treatments [n ((%)]	0	0	0	3 (8.33)	2 (20.00)	0	0	1 (9.09)	0.115
Gap period (months)	NA	NA	NA	15.33 ± 5.03	15	NA	NA	16	NA

Values are means ± SD, unless otherwise indicated.
* *p*-value for the total non-switchers group compared with the total switchers group.
DMT, disease-modifying treatment; EDSS, Expanded Disability Scale Score; F, female; M, male; NA, not available.

Therapeutic effect of existing treatments in MS patients

To compare the efficacy of DMTs and non-DMTs (corticosteroids or immunosuppressive agents) in MS patients in Guangzhou, Southern China, Kaplan-Meier survival analysis was performed. Thirty nine MS patients initially treated with first-line DMTs and 39 MS patients treated initially with non-DMTs (corticosteroids or immunosuppressive agents) were selected. The two groups were matched for sex and the EDSS at initiation of treatment. Kaplan-Meier survival analysis showed that MS patients treated with non-DMTs initially achieved an EDSS of 3.0 more rapidly than patients treated with DMTs initially, but the difference was not statistically significant (99.58 ± 11.33 months vs 125.96 ± 10.66 months, respectively; $p = 0.437$) [Figure 4]. Eighteen highly active MS patients receiving treatment with rituximab for at least one year were included. Follow-up EDSS in these patients was lower than than baseline [2.00 (1.00, 5.38) vs. 1.50 (1.00, 2.00), P = 0.119] though the difference did not reach statistical significance. ARR after treatment decreased than that before treatment [0.74 (0.00, 1.17) vs. 1.50 (0.00, 2.00), P < 0.001].

DISCUSSION

To our knowledge, there is no published literature on the patterns of treatment for MS patients in remission in China. The choice of first-line drugs for MS patients in Guangzhou, Southern China is different from that in western countries. According to our single-center data, treatment of MS patients in Guangzhou can be divided into 3 stages: the first stage which existed before 2015, was when there was only one DMT (INF-β) approved by the CFDA. MS patients were mainly treated with INF-β, corticosteroids or immunosuppressive agents. The second stage which was from 2016 to 2017, was when there were no DMTs in China. MS patients were mainly treated with corticosteroids or immunosuppressive agents during this time. After 2018, when teriflunomide had been approved by the CFDA, MS patients were mainly treated with teriflunomide or immunosuppressive agents. Although previous studies have shown that corticosteroids have no effect on the long-term prognosis of MS [8], we found that the proportion of patients receiving corticosteroid maintenance therapy was relatively high in the earlier years. A considerable proportion of these patients were first seen in local small hospitals, indicating that management of MS lacked standardization in vast

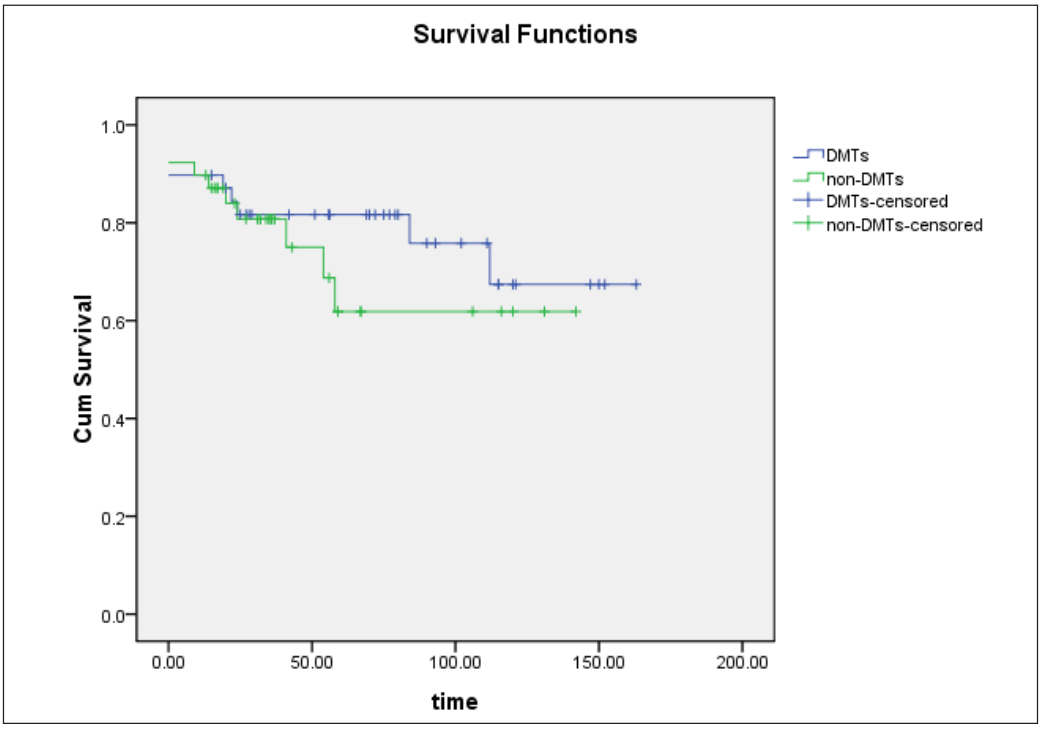

Figure 4. Kaplan-Meier survival analysis of the time to reach an Expanded Disability Status Scale (EDSS) score of 3.0, according the initial treatment.

areas of China during these years. In recent years, however, the proportion receiving corticosteroid maintenance therapy has gradually declined, indicating that Chinese doctors' understanding of MS is increasing gradually.

Compared with the world average level of 50% for the median percentage of people with MS who are eligible to receive DMTs that actually receive them[9] (https://www.who.int/mental_health/neurology/atlas_multiple_sclerosis_resources_2008/en/), the ratio of MS patients who receive DMTs in China is extremely low (0-2% according to previous studies[10-15], and 28.09% at our center). Many patients choose corticosteroids or immunosuppressive drugs. The reasons for the low rate of MS patients receiving DMTs in Guangzhou may be: (1) compared with western countries, the number of DMTs approved for use in China is relatively low ─ only INF-β and teriflunomide; (2) the time that DMTs have been present in the Chinese market is short (INF-β1a was marketed in 2004 but withdrawn in 2010; INF-β1b was marketed in 2010, withdrawn in 2015, and resumed supply in 2018; teriflunomide was not marketed until 2018); (3) some doctors take a wait-and-see attitude at the early stage of patients' disease when the neurological function defect of patients with MS is mild; and arguably most importantly (4) DMTs are too expensive for most MS patients in China. According to the Multiple Sclerosis International Federation, the usage rate of DMTs is associated with economic income. The median percentage of people receiving DMTs in high income countries is 75%; in upper-middle income countries it is 40%, in lower-middle income countries it is 34%, and in low income countries it is 10%[9] (https://www.who.int/mental_health/neurology/atlas_multiple_sclerosis_resources_2008/en/). Taking INF-β1b as an example, patients would need to spend about 80,000 to 100,000 yuan ($11,483) a year without the support of the Chinese government's medical insurance, but the per capita disposable income in China in 2017 was only 25,974 yuan ($3,728), according to the Statistical Bulletin of the National Economic and Social Development of the People's Republic of China in 2017 (issued by the State Bureau of Statistics on February 28, 2018) (http://www.stats.gov.cn/tjsj/zxfb/201802/t20180228_1585631.html), Consequently, most patients with MS cannot afford DMTs due to their economic burden.

In Western countries, drug withdrawal and drug switching rates (9% and 19%, respectively) by MS patients is low.[16] Patients typically stop treatment entirely due to either the inefficacy of the medication, or its adverse effects.[16] Patients with MS whose disease activity is inadequately controlled with traditional first-line therapy may switch to another first-line therapy or to second-line therapies such as natalizumab, fingolimod, etc.[1,16] The MS treatment strategy in Guangzhou, Southern China is different from that in western countries. Because DMTs are few and expensive, only a minority of patients with mild to moderate relapsing MS receive first-line DMTs; others receive corticosteroids or immunosuppressive agents as alternatives for first-line DMTs. For highly active relapsing MS or progressive MS, only a minority of patients choose second-line DMTs by purchasing drugs abroad, while other patients receive treatment with rituximab. MS patients who receive initial treatment with first-line DMTs have higher drug withdrawal rates (32.6%), and drug switching rates (30.43%) than those of western populations. Additionally, in MS patients initially treated with first-line DMTs who switched to other drugs, a gap between treatments was common (8/14; 57.14%). The main reason for higher drug withdrawal and switching rate may be: (1) some doctors advice drug withdrawal and observe if the patient is stable and mild (40.00% of patients initially treated with first-line DMTs discontinued treatment due to doctors' suggestions; (2) many patients can not ensure treatment adherence because of the high cost of treatment; (3) many Chinese patients with MS have no channels to buy drugs. From Figure 1 and Figure 2, in 2016-2017 no INF-β was available, which lead to high withdrawal rate, and patients with initial INF-β treatment decreased from 26% to 2%; (4) treatment delay for MS is another reason. As shown in Tables 2 and 3, MS patients with a high initial EDSS are more likely to switch treatment. Therefore, the time of initiating DMTs in some Chinese MS patients may be later, leading to an increase in the drug switching rate. Consequently, MS patients should be treated at an early stage of the disease when the EDSS is lowest.

The efficacy of DMTs in MS has been confirmed.[1,3] The Kaplan-Meier survival analysis we performed showed that MS patients who receive DMTs initially achieve an EDSS of 3.0 later than patients treated with non-DMTs initially. However the lack of a significant difference in this finding may be due to the fact that many Chinese MS patients treated with DMTs have higher gaps between treatments, and higher drug withdrawal and drug switching rates because of economic reasons or no channels to purchase drugs. Several studies have shown rituximab reduced

inflammatory activity, incidence of relapse, and new lesions on MRI in patients with RRMS and progressive MS.[17-19] Similar to previous studies, rituximab showed some efficacy in highly active MS patients in Guangzhou. We found that EDSS score of MS patients treated with rituximab decreased compared with baseline level (lack of significance may due to the small sample), and ARR decreased after treatment [0.74 (0.00, 1.17) vs. 1.50 (0.00, 2.00), $P < 0.001$]. Rituximab is not currently approved for the treatment of MS and can only be administered off-label for this indication, but it is worth considering for highly active MS population in limited medical-resource countries because of these encouraging results and its cost-effectiveness profile.

Although the number of enrolled patients was limited due to the low prevalence of MS in China, data from our center which is the largest multiple sclerosis center in South China, may represent the current situation of MS treatment in South China to a large extent. Further effects will be required to provide more data from multi-centers on the treatment patterns of MS in China.

In summary, it is still difficult for MS patients to receive prompt DMTs in Guangzhou, Southern China. In future, we expect more DMTs to enter the Chinese market and for these drugs to be supported by medical insurance policies.

We can conclude that DMTs for MS in Guangzhou, Southern China appear to lag behind those in Western countries. Much work is needed to improve drug accessibility and affordability of DMTs in China. Rituximab is an option for highly active MS in limited medical-resource countries.

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DISCLOSURE

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