ORIGINAL ARTICLE

The Use of Disease-Modifying Therapy (DMT) to Prevent Disability Progression in Patients with Multiple Sclerosis (MS) in Thailand

Saharat Aungsumart, PhD, MD[1], Nawarat Kanjanakittichai, MD[1], Metha Apiwattanakul, MD[1]

[1] Department of Neurology, Prasat Neurological Institute, Bangkok, Thailand

Background: Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system that leads to significant disability and economic burden for patients, families, the health system, and society.

Objective: To describe the demographics, natural history, and effectiveness of disease-modifying therapies (DMTs) in MS patients.

Materials and Methods: The present study was a retrospective cohort study of patients diagnosed with MS at the Prasat Neurological Institute, a tertiary referral neurological center in Bangkok, Thailand, between June 1, 2010 and June 30, 2020. Demographic data, clinical characteristics, and disease course of MS patients were explored. The primary outcome of the present study was a comparison of time to events of clinical relapse, new magnetic resonance image (MRI) T2W activity, new MRI T1W with gadolinium (Gd) enhancement, and time to disability progression between patients who received DMT and patients without DMT.

Results: There were 102 patients diagnosed with MS. The female-to-male ratio was 2.4-to-1. The mean age at onset was 29.61±11.62 years. The phenotypic features of these patients were classified as RRMS 80.4%, SPMS 8.8%, PPMS 3.9%, and tumefactive demyelination 6.9%. Forty-eight patients (47.1%) received DMT, 28 (58.3%) received IFN-beta, 11 (22.9%) received fingolimod, seven (14.6%) received teriflunomide, and two (4.2%) received rituximab. Results demonstrated that patients who did not received DMT had significantly more clinical disability compared to patients who received DMT (HR 2.97; 95% CI 1.01 to 8.73; p=0.048). However, the times to clinical relapse and MRI activity, including new T2W and new T1W Gd enhancing lesion, were not significantly different between the two groups.

Conclusion: Patients with a relapsing-remitting phenotype tended to progress to severe disability within ten years. Treatment with DMT may delay disability progression in patients with MS.

Keywords: Multiple sclerosis (MS); Disease-modifying therapy (DMT)

Received 19 December 2022 | Revised 26 January 2023 | Accepted 6 February 2023

J Med Assoc Thai 2023;106(4):393-401

Website: http://www.jmatonline.com

Multiple sclerosis (MS) is a chronic immune-mediated disease of the central nervous system that affects young adults. It has a significant economic and social impact that causes a long-term burden with improper protection and management.

The prevalence of MS is increasing worldwide, with approximately two million cases in 2016. The prevalence and incidence of MS vary among different countries and various geographical areas. Western countries are a higher prevalence region for MS compared to Asia[1]. Although the estimated incidence of MS in Thailand is approximately 1 to 2 per 100,000 for the population, it causes a significant socioeconomic burden.

There is no curative treatment for MS. The targets of care are to improve the quality of life, delay the disability, and reduce the frequency of relapse. Disease-modifying therapies (DMTs) are essential for the management of MS patients to reduce the relapse rates, the magnetic resonance imaging lesion accumulation, and delay the disability with improvements in clinical and quality of life outcomes[2]. The various types of DMTs, such as Alemtuzumab, Natalizumab, and Ocrelizumab, exhibit different efficacies in decreasing the relapse rate to approximately 70% compared with placebo. Fingolimod decreases relapse by 47% to 54% and interferon-beta and teriflunomide decrease relapse

Correspondence to:

Aungsumart S.

Department of Neurology, Prasat Neurological Institute, 312, Thung Phaya Thai, Ratchathewi, Bangkok 10400, Thailand.

Phone: +66-2-3069899, **Fax**: +66-2-3547085

Email: saharatau@hotmail.com

How to cite this article:

Aungsumart S, Kanjanakittichai N, Apiwattanakul M. The Use of Disease-Modifying Therapy (DMT) to Prevent Disability Progression in Patients with Multiple Sclerosis (MS) in Thailand. J Med Assoc Thai 2023;106: 393-401.

DOI: 10.35755/jmedassocthai.2023.04.13824

by 17% to 37%[3].

However, a prior study of MS in Thailand contained insufficient data of DMT in clinical practice because some health coverage schemes restricted the use of DMT. Only 10% to 15% of MS patients in Thailand have access to DMT. The present study determined the natural history, phenotype of the disease, and the effectiveness of DMT in MS patients. The authors also examined the benefits of DMT in control of clinical relapsed and magnetic resonance image (MRI) activity, and confirmed disability progression in routine clinical practice in Thai patients with MS.

Materials and Methods

Patients and study design

The present study retrospectively reviewed medical records between June 1, 2010 and June 30, 2020 in the Prasat Neurological Institute, a tertiary referral neurological center in Bangkok, Thailand. Outpatients and in-patients who fulfilled the diagnostic criteria of MS using the McDonald Diagnosis criteria 2017 and had follow-up visit for at least three months were enrolled in the present study. The exclusion criteria were patients with incomplete medical records, lack of follow-up data, and patients who had a subsequent alternative diagnosis, such as neuromyelitis optica spectrum disorders.

The Ethics committee of Prasat Neurological Institute approved the present study (approval number 63006).

Data collection and analysis

The following patient information were recorded, demographic data, clinical characteristics and disease course of MS from the clinical first attack, age at onset, functional ability of MS patients as defined by the Ordinals of Kurtzke's Expanded Disability Status Scale (EDSS) at onset, MRI activity at onset, oligoclonal band examination, phenotype of disease, type of DMT, disease duration, and annualized relapse rate (ARR). The clinical characteristics in each phenotype were classified into four groups according to the presentation at the last visit as relapsing remitting MS (RRMS), secondary progressive MS (SPMS), primary progressive MS (PPMS), and tumefactive CNS demyelination. Follow-up data were collected at 0, 3, and 6 months or until the end of the observation period, which corresponded with the estimated duration of the treatment effect. Information on adverse events of DMTs was also collected. Meanwhile, patients unable to access DMT in the present study cohort received the immunosuppressive drug as relapse prevention, especially patients with active disease.

The effectiveness of DMTs was determined using the time to events, which included time to clinical relapse. Relapse was defined according to the individual studies, such as worsening or appearance of new neurological symptoms 24 hours or more post-intervention, without evidence of fever or infection. In addition, other outcomes were time to new MRI T2W or the presence of new T2W activity, and time to disability progression, which was defined as an EDSS of 6 points or more for at least 12 weeks by comparing patients who received DMT and patients without DMT.

Statistical analysis

Statistical analyses were performed using SPSS Statistics for Windows, version 17.0 (SPSS Inc., Chicago, IL, USA). For the demographic information, the frequency data were reported as a number with percentage, and continuous data were expressed as means ± standard deviation.

The Kaplan-Meier method was used to estimate the median time to the outcome of interest, including time to first clinical relapse, new MRI T2W activity, new MRI T1W with gadolinium (Gd) enhancement, and EDSS of 6 or more. To determine the effect of DMTs, the parametric survival in the Weibull model was used to compare patients who used DMT and the standard care without DMT for the outcomes of interest. The co-variables included demographic data as age at onset, gender, and health scheme, course of MS as onset, duration, type of MS, and oligoclonal band, severity as number of relapses in one year, and co-morbidity as hypertension, diabetes melilites, and autoimmune disease. Then significant statistical co-variables with p-value less than 0.1 from univariate analysis and important clinical variables from the number of relapses in one year would simultaneously be considered in multivariate parametric survival model. The hazard ratio was calculated as the ratio of two hazard functions, and the cut-off for statistical significance was p-value of less than 0.05.

Results

Demographic data

The medical records of 423 patients diagnosed with MS in the ICD-10 database were reviewed. One hundred one patients were excluded due to unavailable medical records, and 197 patients did not fulfill the diagnostic criteria of MS with 42

Table 1. Baseline characteristics of patients

Basic demographics	RRMS (n=82)	SPMS (n=9)	PPMS (n=4)	Tumefactive (n=7)	Total (n=102)
Sex; n (%)	82 (80.4)	9 (8.8)	4 (3.9)	7 (6.9)	102 (100)
Male	19 (63.3)	5 (16.7)	3 (10.0)	3 (10.0)	30 (29.4)
Female	63 (87.5)	4 (5.6)	1 (1.4)	4 (5.6)	72 (70.6)
Age (years); mean±SD	37.67±13.40	45.29±11.04	44.57±14.40	64.42±17.05	39.37±13.77
Medical history; n (%)					
Hypertension	10 (83.3)	1 (8.3)	0 (0.0)	1 (8.3)	12 (11.8)
Diabetes mellitus	2 (66.7)	1 (33.3)	0 (0.0)	0 (0.0)	3 (2.9)
Dyslipidemia	10 (83.3)	1 (8.3)	0 (0.0)	1 (8.3)	12 (11.8)
Cardiovascular disease	1 (100)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)
Autoimmune disease	2 (100)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.0)
Other	10 (66.7)	0 (0.0)	2 (13.3)	3 (20.0)	15 (14.7)
Race; n (%)					
Thai	80 (80.8)	8 (8.1)	4 (4.0)	7 (7.1)	99 (97.1)
Other	2 (66.7)	0 (0.0)	0 (0.0)	1 (33.3)	3 (2.9)
Family history of MS; n (%)	2 (66.7)	0 (0.0)	0 (0.0)	1 (33.3)	3 (2.9)
Personal history					
Smoking; n (%)	1 (50.0)	1 (50.0)	0 (0.0)	0 (0.0)	2 (2.0)
BMI; mean±SD	22.65±4.81	21.93±6.67	22.64±1.97	23.47±2.58	22.64±4.75

RRMS=relapsing remitting multiple sclerosis; SPMS=secondary progressive multiple sclerosis; PPMS=primary progressive multiple sclerosis; MS=multiple sclerosis; BMI=body mass index; SD=standard deviation

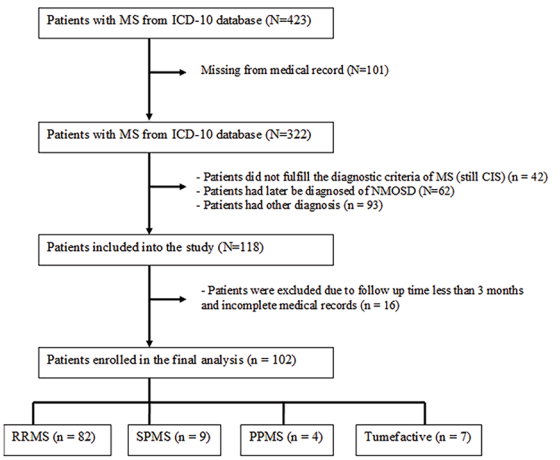

Figure 1. Flow chart of the patients enrolled in the study.

patients that had clinically isolated syndrome (CIS), 62 patients that were diagnosed as NMOSD, and 93 patients that were diagnosed as others. Another 16 patients with incomplete medical records or a follow-up period fewer than three months were excluded. Therefore, 102 patients were enrolled in the final analyses (Figure 1). All patients were separated into four groups by current MS phenotype with 82 (80.4%) that had RRMS, nine (8.8%) that had SPMS, four (3.9%) that had PPMS, and seven (6.9%) that had tumefactive demyelinating disease.

The demographic data are summarized in Table 1. There were 29.4% males and 70.6% female patients, with female-to-male ratio (F:M) of 2.4:1. The F:M ratio was higher in the RRMS subgroup at 3.3:1 compared to the SPMS and tumefactive groups at 1:1. In contrast, PPMS showed a male predominance (F:M of 1:3). A family history of MS presented in three patients (2.9%), of which two of these patients were siblings. Two patients had underlying autoimmune disease (autoimmune hepatitis and Graves' disease). Cigarette smoking was recorded in only two patients, which may be under-recorded due to the inclusion of only active smoking at the present time of clinical evaluation.

Clinical features and disease progression

The average age of all groups was 39.37±13.77 years at the time of the last visit. The age at onset varied between 3 to 63 years (mean of 29.61±11.62 years in RRMS). The mean duration of illness was 7.2 years (mean of 86.92±72.82 months), and the SPMS group had the longest duration of 11.6 years (140.0±59.97 months, range 54 to 277 months). The time to develop SPMS in the present study was 119.0±64 months. The mean EDSS at onset was 3.51±1.51 for the entire cohort. The mean final EDSS for the RRMS patients was 2.11±2.39 months for the DMT and no DMT groups. The mean final EDSS

Table 2. Clinical characteristics and disease progression

Clinical characteristic	RRMS (n=82)	SPMS (n=9)	PPMS (n=4)	Tumefactive (n=7)	Total (n=102)
First clinical presentation; n (%)					
VA failure	18 (90.0)	2 (10.0)	0 (0.0)	0 (0.0)	20 (19.6)
Double vision	8 (100)	0 (0.0)	0 (0.0)	0 (0.0)	8 (7.8)
Weakness	38 (76.0)	6 (12.0)	1 (2.0)	5 (10.0)	50 (49.0)
Sensory loss	39 (84.8)	5 (10.9)	1 (2.2)	1 (2.2)	46 (45.1)
Ataxia	9 (60.0)	3 (20.0)	0 (0.0)	3 (20.0)	15 (14.7)
Dysarthria	0 (0.0)	0 (0.0)	0 (0.0)	2 (100)	2 (2.0)
Stiffness	5 (55.6)	1 (11.1)	3 (33.3)	0 (0.0)	9 (8.8)
Other	8 (88.9)	0 (0.0)	1 (11.1)	0 (0.0)	9 (8.8)
Clinical course and progression; mean±SD					
Age at onset (years)	29.61±11.62	32.04±12.68	37.02±10.13	44.07±15.48	31.10±12.35
Disease duration (months)	86.61±73.39	140.0±59.97	91.75±56.76	19.57±24.32	86.92±72.82
Time to SPMS (months)	-	119.0±64.0	-	-	119.0±64.0
EDSS at onset	3.32±1.33	4.72±2.35	3.75±1.44	4.07±1.64	3.51±1.51
EDSS final	2.11±2.39	7.0±1.0	6.0±0.61	2±2.5	2±3.0
ARR	0.49±0.89	0.02±0.01	0	1.06±1.61	1.0±1.0
First clinical phenotype; n (%)					
CIS	52 (63.4)	3 (33.3)	0 (0.0)	0 (0.0)	55 (53.9)
RRMS	30 (36.6)	5 (55.6)	0 (0.0)	0 (0.0)	35 (34.3)
PPMS	0 (0.0)	1 (11.1)	4 (100)	0 (0.0)	5 (4.9)
Tumefactive	0 (0.0)	0 (0.0)	0 (0.0)	7 (100)	7 (6.9)
Oligoclonal band positive; n (%)	30 (66.7)	4 (66.7)	1 (33.3)	1 (25.0)	36 (62.1)
MRI at first attack; n (%)					
MRI was done at first attack	59 (76.6)	8 (10.4)	3 (3.9)	7 (9.1)	77 (75.5)
MRI brain T2W hyperintensity; n (%)					
1 to 8 lesion	21 (48.8)	3 (75.0)	2 (66.7)	7 (100)	33 (57.9)
≥9 lesion	22 (51.2)	1 (25.0)	1 (33.3)	0 (0.0)	24 (42.1)
MRI brain T1 with Gd enhancement; n (%)					
1 lesion	9 (42.9)	1 (100)	0 (0.0)	7 (100)	17 (54.8)
≥2 lesion	12 (57.1)	0 (0.0)	0 (0.0)	0 (0.0)	12 (38.7)
Disease-modifying therapies; n (%)	Total 48	-	-	-	-
IFN-β	28 (58.3)				
Teriflunomide	7 (14.6)				
Fingolimod	11 (22.9)				
Rituximab	2 (4.2)				
Neurological complications of disease; n (%)					
Spasticity	29 (35.4)	9 (100)	4 (100)	2 (28.6)	44 (43.1)
Pain	26 (31.7)	6 (66.7)	2 (50.0)	1 (14.3)	35 (34.3)
Neurogenic bowel and bladder	18 (22.0)	6 (66.7)	3 (75.0)	0 (0.0)	27 (26.5)
Immobilization	22 (26.8)	9 (100)	4 (100)	2 (28.6)	37 (36.3)
Pseudorelapse or Uhthoff's phenomenon	18 (22.0)	2 (22.2)	1 (25.0)	0 (0.0)	21 (20.6)
Fatigue	22 (26.8)	2 (22.2)	1 (25.0)	1 (14.3)	26 (25.5)
Depression	9 (11.0)	3 (33.3)	2 (50.0)	1 (14.3)	15 (14.7)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

RRMS=relapsing remitting multiple sclerosis; SPMS=secondary progressive multiple sclerosis; PPMS=primary progressive multiple sclerosis; EDSS=Expanded Disability Status Scale; ARR=annualized relapse rate; CIS=clinically isolated syndrome; MRI=magnetic resonance image; Gd=gadolinium; SD=standard deviation

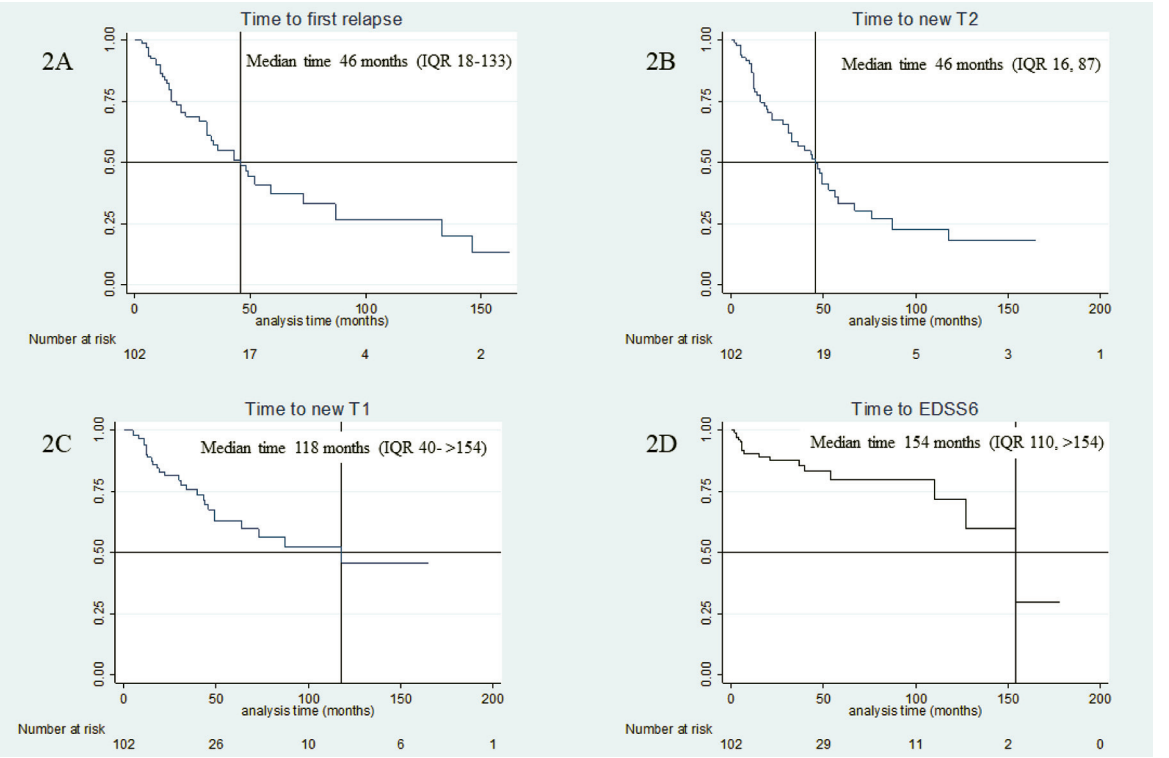

Figure 2. Median time to first clinical event for all MS patients. First clinical relapse (2A), MRI new T2W activity (2B), MRI new T1W with Gd enhancement activity (2C), clinical disability (2D) (define by EDSS ≥6).

in the SPMS group was 7.0±1.0. The mean annual relapse rate was 0.49±0.89 in the RRMS group.

The most common initial presentation in rank order were motor symptoms, sensory symptoms, visual impairment, ataxia, spasticity, and diplopia (Table 2). Cerebrospinal fluid studies for oligoclonal bands (OCB) were obtained in 58 patients (56.9%), and 36 of these patients (62.1%) were positive (Table 2).

Neuroimaging of the brain and spine

MRIs of the brain and spine were carried out at disease onset, during the follow-up or at the time of relapse. At disease onset, 77 patients (75.5%) had MRI and 24 patients (42.1%) showed nine or more T2W lesions. Twenty-nine patients (37.7%) had one or more Gd enhanced lesions. For spinal MRI, 29 patients had short lesions less than three vertebral body segments, and 11 patients showed Gd-enhanced lesions.

Neurological complications of the disease

Spasticity was the most common neurological complication (35.4% in RRMS and 100% in progressive MS) and caused immobilization and beside weakness. Other complications that affected quality of life were pain (34.3%), neurogenic bowel and bladder (26.5%), fatigue (25.5%), and depression (14.7%).

Time to clinical relapse, new T2W lesion, new Gd lesion, and development of EDSS ≥6

The median time to first clinical event is shown in Figure 2. The median time to first clinical relapse and new T2W activity was 46 (IQR 18, 133) months and 46 (IQR 16, 87) months, respectively. The time to a new T1W Gd enhancement lesion was 118 (IQR 40, >154) months, and the time to develop EDSS of 6 or more was 154 months (IQR 110, >154) months.

The effectiveness of DMT in patients with MS

To compare the effectiveness of DMT in MS, all MS patients in the present study cohort were used in the analyses. Forty-eight patients in the cohort received DMTs with 28 (58.3%) who received IFN-beta, seven (14.6%) who received fingolimod, eleven (22.9%) who received teriflunomide, and two (4.2%) who received rituximab. The baseline relapse rate per year were 0.38 (0.56) and 0.71 (1.26) in patients on DMT, and without DMT, respectively. However, after

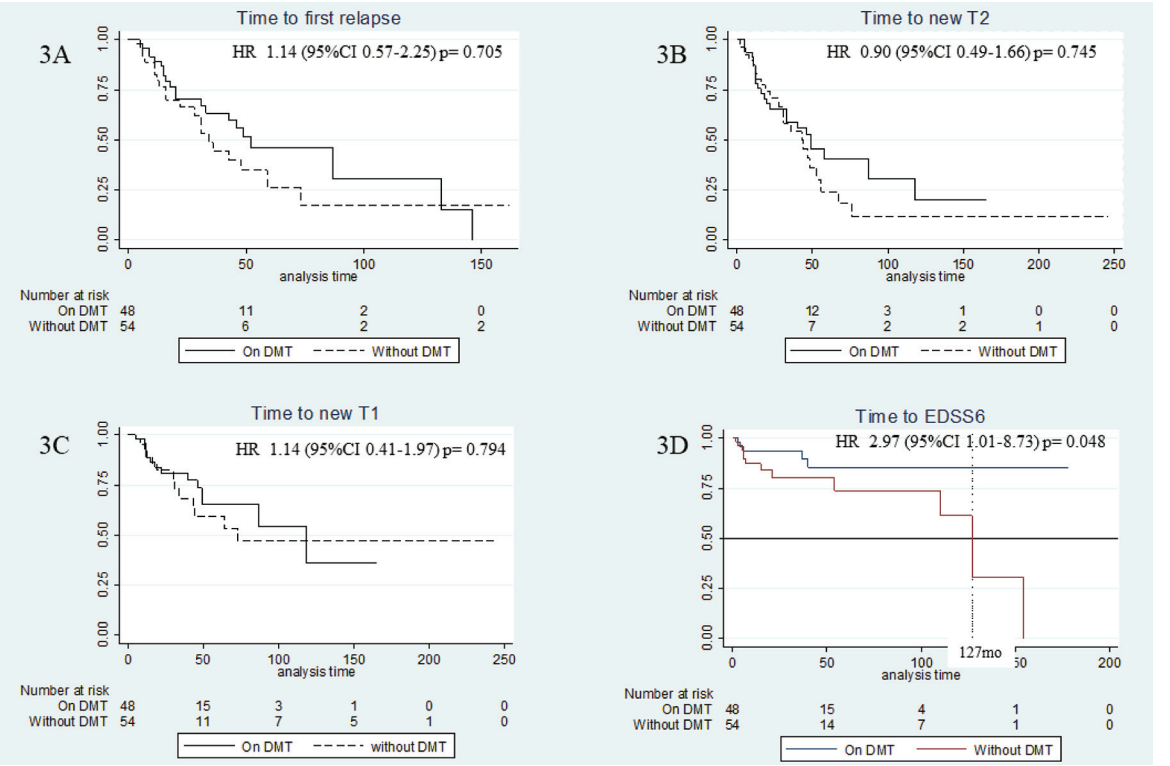

Figure 3. Kaplan-Meier analyses of outcomes. The Kaplan-Meier curves for the time to first event of the primary outcome, defined as first clinical relapse (3A), MRI T2W activity (3B), T1 with Gd enhancement activity (3C), and clinical disability (3D) (defined by EDSS ≥6). Moreover, 50% of patients without DMT progressed to clinical disability in 127 months, and 85% patients in the DMT group did not progress to disability.

Table 3. Adverse effects of disease-modifying therapies

Adverse effects of DMT	IFN-β (n=28); n (%)	Teriflunomide (n=11); n (%)	Fingolimod (n=7); n (%)	All* (n=48); n (%)
Hepatitis	3 (10.7)	0 (0.0)	1 (14.2)	4 (8.3)
Leukopenia	3 (10.7)	0 (0.0)	5 (71.4)	8 (16.7)
Active infection	4 (14.3)	0 (0.0)	1 (14.2)	5 (10.4)
Macular edema	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hair loss	3 (10.7)	3 (27.2)	1 (14.2)	7 (14.6)
Severe injection reaction	13 (46.4)	0 (0.0)	0 (0.0)	13 (27.1)
Flu-like symptom	18 (64.3)	0 (0.0)	0 (0.0)	18 (37.5)
Heart block	0 (0.0)	0 (0.0)	1 (14.2)	1 (2.1)
Skin hyperpigmentation	0 (0.0)	0 (0.0)	4 (57.1	4 (8.3)

DMT=disease-modifying therapy

* Two patients, received rituximab, did not exhibit adverse events

adjusting the age of onset, gender, and baseline relapse rate, which apply into all outcomes, the patients who received DMT therapy exhibited significantly delayed development of clinical disability compared to patients without DMT (HR 2.97, 95% CI 1.01 to 8.73, p=0.048) (Figure 3D). Although, the time to clinical first relapse tended to be delayed in the DMT group, it was not statistically significant (HR 1.14, 95% CI 0.57 to 2.25, p=0.705). The time to develop first T2W and T1W with Gd activity was also not different between the DMT group and the non-DMT group. The time to develop EDSS of 6 or more was demonstrated using the Kaplan-Meier curve (Figure 3D). It showed that 50% of patients without DMT progressed to EDSS of 6 or more in 127 months, but only 15% of patients with DMT developed EDSS

of 6 or more during the same period of time.

Adverse events were observed in each subgroup of patients with DMT (Table 3). The most common side effects in patients received IFN-beta were flu-like symptoms (72.0%), followed by injection-site reactions (52.0%), and systemic infection (16.0%). Flu-like symptoms were mild and improved with supportive treatment. An increase in liver enzymes, leukopenia, and hair loss were found in only three patients (12.0%). Three patients (37.5%) of the patients that received teriflunomide had hair loss and one patient discontinued the drug due to the severity of hair loss. Thirty-three-point-three percent of the patients who received fingolimod showed a decrease in white blood cell count. However, the effects of leukopenia were transient, and no changes to drug dosage or discontinuation were recorded. Skin hyper-pigmentation was found in four patients, but it did not progress to malignant lesions. Hepatitis, systemic infection, hair loss, and heart block were each found in a single patient.

Discussion

The gender distribution, age of disease onset, the first symptoms, and the distribution of clinical disease phenotypes in the present study are consistent with the globally accepted pattern of the course of MS. However, the patients had a few clinical spectra that differed from the Western countries. The female-to-male ratio in the present study was 2.4:1, which is lower than the prior Thai study of Siritho et al.[4] at 6.2:1, but similar to another report of MS in Asians[5]. The mean age of first MS manifestation was 31.10±12.35 years, which corresponds with the data of Tremlett et al.[6]. However, the mean age of onset was slightly lower in the RRMS group at 29.61±11.62 years. Among all patients, three patients (2.9%) had a family history of MS, but Sasitho et al. had no reports of MS among Thai families. Genetic loading is associated with a shorter time to secondary progressive MS and a younger age for primary-progressive MS[7]. Cigarette smoking is associated with an increased risk of MS[8], but only 2% of MS patients smoked in the present study. This difference may be explained by the under-detection of smoking due to the retrospective nature of the study.

The clinical manifestations at disease onset were mostly motor deficit (49%), followed by sensory deficit (45.1%) and optic neuritis (19.6%). This result is different from the prior study in Thailand[9], which found that optic neuritis was a major symptom, followed by weakness. This evidence suggests that disease progression has changed from the past. The first clinical manifestation of a motor deficit was associated with a faster conversion to SPMS, but the disease onset as optic neuritis was associated with a slower conversion to SPMS[10]. These results indicate that the use of DMTs should be administered earlier than the previously published guideline[11]. Before the availability of the approved DMTs, studies showed that 50% of patients diagnosed with RRMS would transition to SPMS within 10 years, and 90% would transition within 25 years[12]. These data are similar to the present study results. The patients who did not receive DMTs showed confirmed disability progression at 119±64 months, or almost 10 years, and the group that received DMTs had only 20% progression to EDSS 6 within the same period. Therefore, the data support that DMT is a critical component of the management of patients with MS. These results were also confirmed in previously published studies[13].

The evidence in clinical trials support the use of DMTs in MS patients, which reduces the time to clinical relapse and MRI lesion accumulation and was associated with improvements in clinical and quality-of-life outcomes[14]. The present study results did not show significant differences in the time to clinical relapse or active MRI activity. Clinical relapse and active MRI lesions in patients with MS are inevitable, especially in long-term follow-up. The present study results differed from clinical trial and systematic reviews, in which DMT is clearly effective in preventing MS relapse and MRI activity[15,16]. Two reasons might explain the diminished clinical effectiveness of the present study. The first one is that most of the cohort patients used first-line DMT, which is considered low efficacy. In addition, the long-term follow-up study and real-world setting affected many uncontrol factors such as adherence, side effect, or breakthrough disease. These all-possible factors contribute to the loss of effectiveness of DMT in the long run, which is similar to various disease treatments in the real-world setting[17]. However, the present study findings indicate that DMT might halt disease progression, which is essential for a patient's quality of life.

The benefit of DMT in disability prevention in MS patients in the Thailand healthcare system is a paramount concern. Although the burden of MS on patients and their families has been recognized for over 20 years, the healthcare system does not cover DMT cost because it is not listed in the national list of essential medicines (NLEM). The unequal health

coverage schemes lead to access to DMT for only a minority of patients, the Civil Servant Medical Benefit Scheme (CSMBS). The high cost of DMTs is a barrier for accessibility to DMTs for Thai MS patients[18]. The main finding of the present study result indicates that DMT is a main factor to slow progression in MS patients. The slowing of the disability progression improves the quality-of-life of patients and their families. MS affects patients' health-related quality of life and functioning, and the symptoms of MS pose a significant economic burden on patients, families, the health system, and society, with higher direct and indirect costs incurred with increasing levels of disease severity and progression[19]. MS patients are middle-aged and have the potential to work and gain income for the country. However, the health and economic impact are increased if these patients develop disabilities.

Adverse events from DMTs, such as flu-like symptoms, injection site reactions, and leukopenia, were reported in some cases. These reactions were mild. There were no serious adverse events in the present study. The adverse events that occurred in Thai patients were hair loss for 37.5%, but other studies found just hair thinning of approximately 2%[20]. Therefore, the choice of teriflunomide use should be discussed with patients before initiation.

The present study has limitations. First, the study was a retrospective study. Data is potentially missing. Second, it may have recall biases in several factors and outcome measurements.

Conclusion

MS has a high burden of illness. Most relapsing remitting patients tend to develop a progressive phase within 10 years. Disability affects patients' health-related quality of life and functioning and causes a significant economic burden on patients, families, the health system, and society. The early use of DMTs delays the disability. Future clinical studies on cost-utility analyses of generic or lower-cost DMTs should be considered to support the use of DMTs to delay disability in MS patients.

What is already known on this topic?

MS is a chronic immune-mediated disease of the central nervous system that cause disability especially for young adult and leads to economic burden. Clinical manifestation of MS evolution over time and criteria of diagnosis has been established. DMT is considered as standard treatment of MS to prevent relapse and disability progression.

What this study adds?

The characteristics of Thai MS patients were similar to the global MS report in term of clinical presentation, MRI lesion, and disability progression. Although DMTs are considered a standard treatment, only half of patients with MS in Thailand had access to the medication. Thai MS patients that do not have access to DMT have a higher chance to develop severe disability. This study highlights the important role of DMT to prevent disability in MS patients.

Acknowledgement

The present study was financially supported by Grant No. 630006 from the Prasat Neurological Institute, Department of Medical Services, Ministry of Public Health, Thailand.

Conflicts of interest

The authors declare no conflict of interest.

References

1. Kingwell E, Marriott JJ, Jetté N, Pringsheim T, Makhani N, Morrow SA, et al. Incidence and prevalence of multiple sclerosis in Europe: a systematic review. BMC Neurol 2013;13:128.
2. Nicholas J, Boster A, Wu N, Yeh WS, Fay M, Kendter J, et al. Comparison of disease-modifying therapies for the management of multiple sclerosis: Analysis of healthcare resource utilization and relapse rates from US Insurance Claims Data. Pharmacoecon Open 2018;2:31-41.
3. Zimmermann M, Brouwer E, Tice JA, Seidner M, Loos AM, Liu S, et al. Disease-modifying therapies for relapsing-remitting and primary progressive multiple sclerosis: A cost-utility analysis. CNS Drugs 2018;32:1145-57.
4. Siritho S, Prayoonwiwat N. A retrospective study of multiple sclerosis in Siriraj Hospital, Bankok, Thailand. Can J Neurol Sci 2007;34:99-104.
5. Eskandarieh S, Heydarpour P, Minagar A, Pourmand S, Sahraian MA. Multiple sclerosis epidemiology in East Asia, South East Asia and South Asia: A systematic review. Neuroepidemiology 2016;46:209-21.
6. Tremlett H, Yinshan Z, Devonshire V. Natural history of secondary-progressive multiple sclerosis. Mult Scler 2008;14:314-24.
7. Tremlett H, Zhao Y, Rieckmann P, Hutchinson M. New perspectives in the natural history of multiple sclerosis. Neurology 2010;74:2004-15.
8. Rosso M, Chitnis T. Association between cigarette smoking and multiple sclerosis: A review. JAMA Neurol 2020;77:245-53.
9. Siritho S, Prayoonwiwat N, Pulkes T, Chankrachang S, Laptikultham S, Nidhinandana S, et al. A retrospective

study of multiple sclerosis in Thailand. 2010;15:253-61.
10. Rzepiński Ł, Zawadka-Kunikowska M, Maciejek Z, Newton JL, Zalewski P. Early clinical features, time to secondary progression, and disability milestones in Polish multiple sclerosis patients. Medicina (Kaunas) 2019;55:232.
11. Ghezzi A. European and American guidelines for multiple sclerosis treatment. Neurol Ther 2018;7:189-94.
12. Weinshenker BG, Bass B, Rice GP, Noseworthy J, Carriere W, Baskerville J, et al. The natural history of multiple sclerosis: a geographically based study. I. Clinical course and disability. Brain 1989;112(Pt 1):133-46.
13. Claflin SB, Broadley S, Taylor BV. The effect of disease modifying therapies on disability progression in multiple sclerosis: A systematic overview of meta-analyses. Front Neurol 2018;9:1150.
14. Brown MG, Kirby S, Fisk JD, Sketris IS, Hoch J, Bhan V, et al. Clinical effectiveness and health outcomes of disease modifying treatment (DMT) that delays disability progression in relapsing/remitting-onset multiple sclerosis:: nova scotia "real world evidence". Value Health 2006;9:A79.
15. Brownlee WJ, Wolf C, Hartung HP, Dingermann T, Anshasi N, Clark RA, et al. Use of follow-on disease-modifying treatments for multiple sclerosis: Consensus recommendations. Mult Scler 2022;28:2177-89.
16. Śladowska K, Kawalec P, Holko P, Osiecka O. Comparative safety of high-efficacy disease-modifying therapies in relapsing-remitting multiple sclerosis: a systematic review and network meta-analysis. Neurol Sci 2022;43:5479-500.
17. Cuzick J. The importance of long-term follow up of participants in clinical trials. Br J Cancer 2022 Dec 1. doi: 10.1038/s41416-022-02038-4.
18. Chanatittarat C, Chaikledkaew U, Prayoonwiwat N, Siritho S, Pasogpakdee P, Apiwattanakul M, et al. Cost-utility analysis of multiple sclerosis treatment in Thailand. Int J Technol Assess Health Care 2018;34:584-92.
19. Naci H, Fleurence R, Birt J, Duhig A. Economic burden of multiple sclerosis: a systematic review of the literature. Pharmacoeconomics 2010;28:363-79.
20. Confavreux C, O'Connor P, Comi G, Freedman MS, Miller AE, Olsson TP, et al. Oral teriflunomide for patients with relapsing multiple sclerosis (TOWER): A randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Neurol 2014;13:247-56.