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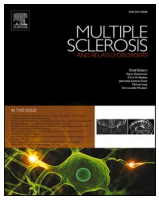

Original article

Economic evaluation of cladribine tablets in high disease activity (HDA) relapsing multiple sclerosis (RMS) patients in Lebanon

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ABSTRACT

Background: Cladribine tablets are a newly launched short course oral treatment approved for high disease activity (HDA) relapsing multiple sclerosis (RMS). The current analysis assessed the cost-utility and budgetary impact of introducing cladribine tablets in HDA-RMS patients compared with other HDA-RMS therapies in Lebanon.

Methods: The global cost-utility and budget impact models were adapted from Lebanese National Social Security Fund (NSSF) perspective. The data for the models' adaptation were retrieved from the literature and validated by Lebanese experts. The comparators considered in the cost-utility model were alemtuzumab, fingolimod, and natalizumab while budget impact analysis additionally considered dimethyl fumarate. A sensitivity analysis was also performed to assess the uncertainty in the analysis.

Results: The cost-utility results showed that cladribine tablets are an economically dominant therapeutic strategy (i.e., less costly and better quality-adjusted life year [QALY]) compared to all comparators. The cost saving was driven by drug acquisition, administration, and monitoring costs; while incremental QALY gain was driven by differences in delayed Expanded Disability Status Scale progression. Sensitivity analysis showed that cladribine tablets have a high probability (99.3–100%) of being dominant at a threshold of 22,000 United States Dollars (approximately three times of gross domestic product) per QALY gained against different comparators. The budget impact analysis showed that the introduction of cladribine tablets would result in 5.0% to 21.5% savings in the overall budget over a period of five years.

Conclusions: Cladribine tablets are a cost-effective and a budget-saving treatment option for the treatment of HDA-RMS patients in Lebanon from the NSSF perspective.

1. Introduction

Multiple Sclerosis (MS) is a disease of the central nervous system which causes demyelination (disruption of the myelin that insulates and protects nerve cells) of nerve cells in the brain and the spinal cord. Due to the loss of myelin, the ability of axons to conduct impulses is diminished or lost; thus, patients develop symptoms. Signs and symptoms of MS vary among patients according to the location of the affected nerve fibers. MS is associated with a substantial medical cost and exerts a high burden on society (Karampampa et al., 2012). In 2018, around 2.5 million people around the globe were affected by MS (MS Trust, 2021). A meta-analysis conducted in 2015 showed that MS prevalence in the Middle East was 51.5/100,000 (Heydarpour et al., 2015). In Lebanon, a national study estimated that the total number of MS patients in 2008 was between 1200 and 1700 out of a total population of 4.8 million (Yamout et al., 2008).

Clinically, MS is divided into relapsing disease and progressive disease. In Lebanon, relapsing MS (RMS) was observed in 85.1% of MS patients at diagnosis, while primary progressive MS (PPMS) was observed in 7.9% of the patients. The mean age of Lebanese MS patients

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at onset was reported to be 30.2 years (Yamout et al., 2008). Patients who experience frequent relapses or disability progression are classified as having high disease activity relapsing MS (HDA-RMS) (Hettle et al., 2018). There is no universally accepted definition for HDA-RMS. Based on the summary of product characteristics (SmPC) of cladribine tablets, HDA is defined as at least 2 disabling relapses in one year, and at least 1 Gadolinium (Gd+) enhancing lesions on brain MRI or a significant increase in T2 lesion load as compared to a previous recent MRI. The HDA-RMS patient population is of primary interest in this study (European Medicines Agency. Mavenclad, 2017, 2022).

In the absence of any curative treatment till date, the target for all MS pharmacological therapies is to reduce the risk of relapse and disability progression; such therapies are known as disease modifying drugs (DMDs) (Torkildsen et al., 2016). Presently, more than 10 DMDs are approved for the treatment of MS worldwide (Olek and Mowry, 2022). Most of the DMDs are associated with certain administration and/or monitoring costs as well as potentially serious adverse events (Scolding et al., 2015; Pardo and Jones, 2017). In Lebanon, the treatment options of RMS include immunomodulatory agents such as interferons (IFN), and immunosuppressive agents such as natalizumab and fingolimod (Shatila et al., 2013).

Recently, cladribine tablets were approved in Lebanon for the treatment of the HDA subpopulation of RMS. Cladribine is hypothesized to act as an immune reconstitution therapy (IRT) that offers an alternative to continuous immunosuppression (Giovannoni, 2017). The safety and efficacy of cladribine in RMS were assessed in the CLARITY, CLARITY EXT, ORACLE MS and ONWARD studies (European Medicines Agency. Mavenclad, 2017; Giovannoni et al., 2018; Giovannoni et al., 2010; Leist et al., 2014; Montalban et al., 2018). With a favorable benefit-risk profile, cladribine delivers up to four years of disease control with a maximum of 20 days of oral treatment over 2 years, as indicated by two pivotal trials (CLARITY and CLARITY EXT) (European Medicines Agency. Mavenclad, 2017). The CLARITY EXT study demonstrated that over 75% of patients treated with cladribine in years 1 and 2 remained relapse-free without active treatment in years 3 and 4 (Hettle et al., 2018; Giovannoni et al., 2018). MS patients can benefit from treatment with cladribine over a longer period - extending up to four years- with a lower monitoring burden than other DMDs (Giovannoni, 2017). The objective of the present study was to assess the financial impact and cost-utility of cladribine tablets versus other DMDs in the treatment of HDA-RMS from the Lebanese National Social Security Fund (NSSF) perspective.

2. Methods

The cost-utility analysis (CUA) and budget impact analysis (BIA) models of cladribine tablets, were locally adapted from Lebanese NSSF perspective based on Hettle et al. (2018). An ad hoc literature review was conducted to retrieve data inputs required for the adaptations. Additionally, a discussion guide was developed, to collect experts' opinion on the data gaps and to validate the data retrieved from the literature.

2.1. Cost-utility analysis

2.1.1. Study population and comparators

The baseline characteristics used in the model were derived from data provided by 3 key MS experts in Lebanon. The mean age, weight, and female to male ratio used in the model were 37.7 years, 70 kg, and 2:1, respectively. Other baseline characteristics such as the number of relapses were obtained from the placebo arm of the CLARITY study and were further validated by the key experts. Based on the key experts' inputs, the comparators considered in the study were alemtuzumab, fingolimod, and natalizumab.

2.1.2. Model structure

A Markov state transition model was adapted from Hettle et al. (2018) to estimate the lifetime costs and utility of cladribine tablets and other comparators in HDA-RMS patients. Incremental cost-utility was measured in terms of the incremental cost per quality-adjusted life year (QALY) gained. The willingness to pay (WTP) threshold of 22,000 United States Dollars (USD) (approximately three times the gross domestic product [GDP] per capita) per QALY gained was used to assess the cost-utility (1 USD = 1507.50 Lebanese Pound or LBP on the first of October, 2019). The CUA considered a 50-year time horizon with both costs and QALYs discounted at a rate of 3.5% per annum (Osenenko et al., 2016).

The Markov model was based on two mathematical models:

(1) A natural history reference model developed using data on the disability and relapse status of MS patients receiving best supportive care (BSC) (Siddiqui et al., 2018).
(2) A treatment-adjusted model combining the natural history reference model with data on the comparative efficacy and safety of treatment versus placebo (Siddiqui et al., 2018).

The reference and treatment-adjusted models were based on Kurtzke's Expanded Disability Status Scale (EDSS) system to simulate the costs and utilities for the treatment of HDA-RMS patients. The model, which incorporated a structure of eleven health states (comprised of ten health states and one death state), was taken from British Columbia natural history dataset and was validated by key experts (Kurtzke, 1983). The annualized cycle period was used to predict EDSS score over a lifetime horizon following approaches used in previous economic analyses (Siddiqui et al., 2018; Tappenden et al., 2009; Palace et al., 2015). In each cycle, the cohort was at risk of disability progression (moving to a higher EDSS score); improvement in disability status (moving to a lower EDSS score), remaining at their current level of disability (remaining at their current EDSS score) or death.

2.1.3. Model inputs

Clinical. The clinical inputs used in the CUA were transition probability, relapse rate, mortality rate, and inputs related to the treatment such as comparative efficacy, waning effect, adverse events, and probability of discontinuation. The model used natural history transition probability matrices similar to Hettle et al. (2018) and Palace et al. (2014). For detailed inputs on natural history probabilities refer to Supplementary Table 1. An adjustment parameter (AP = 1.686) was applied prior to adjustment for the effect of DMDs, to increase the probability of annual EDSS progression in the active RMS natural history model in line with the assumption of Hettle et al. (2018).

The CUA incorporated the option to include the annualized relapse rate (ARR) as a function of EDSS. The rate corresponding to each EDSS state was applied to the number of patients occupying that state in each model cycle. The model used default data from the UK risk sharing model that was derived from a 2002 survey by the UK MS trust (Tappenden et al., 2001). The mean duration of each relapse event was obtained from data collected in the CLARITY study (Giovannoni et al., 2010).

The efficacy of DMDs versus placebo for 6 months, in terms of confirmed disease progression (CDP) and ARR, were estimated by meta-regression using random effect model. Following previous NICE appraisals, the waning effect on the long-term benefits of DMDs was used to reflect uncertainty in the efficacy of therapies (Hettle et al., 2018). For all DMDs, the effect was assumed to gradually decrease over time; with 100% of effect maintained in years 0–2, 75% of effect in years 2–5, and 50% of effect from the fifth year onwards; in line with NICE methodology (Hettle et al., 2018). The mortality rate was assumed to vary over time to account for the aging of the cohort. The risk of mortality was

derived by inflating all-cause gender-averaged and age-matched mortality statistics that were inflated to account for the higher mortality rate associated with MS (World Health Organization WHO, 2018).

Patients on DMDs, including cladribine tablets, are at high risk of discontinuing treatment due to loss of efficacy and tolerability, and development of SPMS. It was assumed that any patient with EDSS state ≥7.0 would progress towards SPMS and hence considered discontinued from therapy. This assumption was validated by key experts as per their local practice. Drug discontinuation rates were derived from a network meta-analysis (NMA) of all-cause discontinuation data in RMS (Siddiqui et al., 2018). The probability of drug-related adverse events including infusion site reactions, injection site reactions, progressive multifocal leukoencephalopathy, macular edema, malignancy, hypersensitivity, gastrointestinal disorders, autoimmune thyroid-related events, immune thrombocytopenic purpura (alemtuzumab only), severe infections and influenza-like symptoms; were modeled based on a previously published systematic literature review (Tappenden et al., 2009).

Utilities. The model includes the impact of disability progression, relapse rates, and drug-related adverse events on the health-related quality of life of MS patients. EDSS-related health state utilities (HSU) were taken from the study conducted by Hawton et al in 2015 as well as the CLARITY study (Giovannoni et al., 2010; Hawton and Green, 2016). A utility decrement of -0.071 was assigned per relapse event (Orme et al., 2007). EDSS-related utility loss for caregivers and per adverse event was also included based on previous studies (Acaster et al., 2013; Matza et al., 2015; Trogdon et al., 2016). For detailed utility inputs, refer to Supplementary Table 2.

Costs. The total cost included drug acquisition, drug administration, drug monitoring and management cost of adverse events. These costs were assumed to be incurred for the duration during which patients remained on therapy. This was applied to all treatment-eligible patients after excluding patients who progressed to EDSS ≥7.0, those who progressed towards SPMS, or those who may not tolerate any drug therapy. Drug acquisition costs in 2018 and 2019 were obtained from Lebanon National Drugs Database. The drug administration and drug monitoring costs were based on the average prices paid for healthcare services (HCS) provided in Lebanon hospitals, which were derived from the NSSF. The administration and monitoring costs included the cost related to physician visits, and treatment. (Supplementary Tables 3 to 5)

The adverse event management cost for various DMDs included cost of injection site reaction, progressive multifocal leukoencephalopathy, severe infections, macular edema, gastrointestinal disorder, hypersensitivity reaction and autoimmune thyroid-related events, influenza-like symptoms, malignancy and immune thrombocytopenic purpura. The adverse event cost was based on average prices paid for HCS provided in Lebanon hospitals, derived from expert interviews. The costs of infusion-based adverse events were set to zero on the basis that it was largely covered by the day case admission.

Annualized direct medical costs were assigned to each EDSS health state based on a previous literature review. The relapse costs for non-hospitalized and hospitalized events were assumed at 707 USD and 6,600 USD, respectively (Hawton and Green, 2016).

Sensitivity analyses. Deterministic sensitivity analysis (DSA) identified parameters that exert a significant influence on the model results, through varying individual input values and capturing the model results for each new evaluation. Each parameter considered in the DSA was varied by a fixed amount (50%). The DSA was performed on the following variables: effect of DMD on disease progression and relapse rate, discontinuation rates, mortality multiplier, baseline characteristics (age, weight, female to male ratio), and discounting rates.

Probabilistic sensitivity analysis (PSA) assessed the variation in results stemming from the uncertainty in each individual model parameter. This involved assigning a probabilistic distribution to each model input to randomly select new plausible values. Each new sampled value was applied in the model, and the results of each analysis were recorded. This process was then repeated for 1000 iterations. The series of results recorded in the PSA were then summarized and used to quantify the expected result and variation in results under uncertainty. To assess whether the PSA had converged, the mean total costs and QALYs generated from the analysis were compared to the results of the deterministic analysis.

2.2. Budget impact analysis

Budget Impact Analysis (BIA) assessed the overall financial implication of introducing cladribine tablets for the treatment of HDA-RMS patients across Lebanon over a five-year time horizon. It included costs associated with drug acquisition, drug monitoring, drug administration, adverse events' management, and relapse events.

General inputs that were used in the BIA model:

- Baseline characteristics – The baseline characteristics used in the model were obtained by Lebanon specific expert interviews. Based on experts' opinion, patients' average weight was considered 70 kg based on the calculated average dosing for cladribine tablets. Patient average weight was obtained and validated from key experts.
- Population size – Based on the inputs of the Lebanese experts, HDA-RMS population was estimated by adding up the number of prevalent and incident cases. The annual growth in the RMS population was applied based on Lebanon's specific population growth rate.
- Comparators and scenario analysis: The BIA calculated the total budget impact of introducing cladribine tablets as compared with fingolimod, natalizumab, alemtuzumab and dimethyl fumarate in two scenarios:
  (1) Scenario 1 (partial displacement): In this scenario, the cladribine tablets' market share was subtracted from the shares of other DMDs over the 5-year period based on the experts' assumptions of the market evolution in the coming 5 years.
  (2) Scenario 2 (total displacement): In this scenario, all market share was shifted to cladribine tablets over the 5-year period.
- Market shares – Market shares of cladribine tablets and all the comparators considered for HDA-RMS patients were based on experts' opinion and percentage of each regimen was calculated and included in the model. Based on the experts' opinions, cladribine tablets are likely to capture different proportions of market share from all DMDs.
- Drug and non-drug cost – Drug acquisition cost was included in drug cost while costs associated with drug administration, drug monitoring, adverse events and relapse events were included in non-drug cost. In line with CUA, drug acquisition costs were obtained from Lebanon National Drugs Database. The costs pertaining to drug administration, drug monitoring, and adverse and relapse events were based on the average prices paid for HCS provided in Lebanon hospitals, which were obtained from NSSF. (Supplementary Tables 3 to 5).
- Currency – All cost-related inputs used were in USD.

3. Results

3.1. Cost-utility analysis

3.1.1. Base case scenario

The results demonstrated that cladribine tablets were dominant as compared with other DMDs (alemtuzumab, fingolimod, and natalizumab). Cladribine tablets provided potential cost savings in addition to improved outcomes (i.e. less costly and more effective in terms of incremental QALY). Table 1 shows the results of the base case cost-effectiveness analysis.

Table 1
Results of the base case cost-effectiveness analysis.

Total discounted Intervention	Costs (USD)	LY[a]	QALY[b]	Incremental (cladribine tablets vs.) Costs	% Costs	LY[a]	QALY[b]
Cladribine tablets	234,204	20.225	7.186		Reference		
Alemtuzumab	272,143	20.225	6.947	-37,939	-13.4%	0	0.238
Fingolimod	303,629	20.225	6.150	-69,424	-15.6%	0	1.035
Natalizumab	300,097	20.225	6.546	-65,893	-52.9%	0	0.639

[a] LY; Life Years.
[b] QALY; quality-adjusted life year.

Table 2 describes the detailed cost breakdown of the CUA base case results. The cost difference of cladribine tablets was driven majorly by cost differences in drug acquisition, administration and monitoring. Cladribine tablets were not associated with any administration cost.

3.1.2. Sensitivity analysis

Deterministic sensitivity analysis. The results of DSA demonstrated that a significant influence on the base case results were obtained by varying confirmed disability progression, discounting of cost and outcomes for 50 years. Overall, the DSA has shown that the model's results were robust to the parameter variation in the model. The results of DSA were presented as a tornado diagram of the incremental net health effects comparing cladribine tablets versus fingolimod (Fig. 1). To maintain brevity, the DSA is presented for the comparator with the highest market share in Lebanon (i.e. fingolimod only). The threshold value used for DSA was set to 22,000 USD (approximately 3*GDP per capita).

ARR annualised relapse rate, DP disease progression

Probabilistic sensitivity analysis. The PSA results demonstrated that the cladribine tablets had the highest (100%) probability of being cost-effective at a threshold of 22,000 USD per QALY gained as compared to fingolimod (drug with the highest market share). A detailed comparison of PSA results for cladribine tablets as compared to different comparators is shown in Table 3.

3.2. Budget impact analysis

The BIA assessed the overall budgetary impact over five years in two scenarios - scenario 1 (partial displacement) and scenario 2 (total displacement) in the market across Lebanon.

In scenario 1 (partial displacement), the introduction of cladribine tablets for the treatment of HDA-RMS patients demonstrated cumulative cost savings of 5.0% (~1.3 million USD) over five years. Similarly, in scenario 2 (total displacement), the introduction of cladribine tablets showed cumulative cost savings of 21.5% (~5.5 million USD) over five years. Based on the level of reimbursement from NSSF for the different costs taken into consideration in the BIA, 95% of the cumulative budget is NSSF budget, and the remaining 5% is patient's out-of-pocket budget. The overall impact on the budget in both scenarios is shown in Fig. 2.

In scenario 1 (partial displacement), upon the introduction of cladribine tablets, the greatest percentage of cost reduction was observed in administration cost (42.2%), followed by monitoring cost (26.5%). However, in terms of absolute cost, the major driver for cost-saving is drug acquisition cost (~948,222 USD). Similarly, in scenario 2 (total displacement), the highest percentage of cost reduction was observed in monitoring cost (62.1%) followed by adverse event management cost (40.2%). However, in terms of absolute cost, the major driver for cost-saving is drug acquisition cost (~4,634,314 USD). As an oral formulation, the introduction of cladribine tablets reduced the administration cost to zero. Table 4 shows a breakdown of total drug and non-drug cost for Scenario 1 (partial displacement) and Scenario 2 (total displacement).

4. Discussion and conclusion

This study presents the cost-utility as well as the financial implications of introducing cladribine tablets for the management of HDA-RMS patients in Lebanon from the NSSF perspective. The comparators considered in the CUA were alemtuzumab, fingolimod, and natalizumab. In addition to those comparators, dimethyl fumarate was also considered for the BIA. The BIA considered two scenarios – firstly, partial displacement of other DMDs and secondly, total displacement of other DMDs with the introduction of cladribine tablets.

The results of the base case analysis demonstrated that treatment with cladribine tablets was a dominant option as compared to other DMDs in HDA-RMS patients at a threshold of 22,000 USD per QALY gained (i.e. less costly and more effective in terms of increased QALYs). This can be attributed to the oral posology of cladribine tablets where the treatment effect is expected to last for up to 4 years with only 2 years of treatment (Hawton and Green, 2016) with no costs of administration and lower monitoring costs compared to other drugs.

The predicted lifetime QALY gains on cladribine treatment ranged from 0.238 to 1.035 versus other DMDs. The results from DSA showed that the evaluation is most sensitive to confirmed disability progression. The highest probability of cladribine tablets being a dominant treatment option for HDA-RMS patients was reported in comparison to fingolimod and natalizumab (100%), while the lowest probability was reported against alemtuzumab (99.3%).

The budgetary analysis showed that the potential cost savings ranged from 1.3 million USD to ~5.5 million USD in comparison to different DMDs within the 5-year time horizon. The BIA demonstrated that the introduction of cladribine tablets across Lebanon for the treatment of HDA-RMS patients would be a cost saving option, with 5.0% to 21.5% reduction in total budget within the 5-year time horizon. In terms of absolute value, the major driver of cost savings was drug acquisition cost in partial displacement scenario as well as in total displacement scenario with incremental cost of -948,222 USD and -4,634,314 USD,

Table 2
Cost breakdown of base case results.

Intervention	Acquisition cost (USD)	Administration cost (USD)	Monitoring cost (USD)	Adverse Event cost (USD)	Relapse & Rescue cost (USD)	EDSS- Direct cost (USD)	Total (USD)
Cladribine tablets	67,026	0	420	1047	3,570	162,141	234,204
Alemtuzumab	99,228	764	4,724	1096	3,689	162,643	272,143
Fingolimod	132,849	56	1,174	1007	4,191	164,351	303,629
Natalizumab	126,215	4012	1,309	999	4,067	163,495	300,097

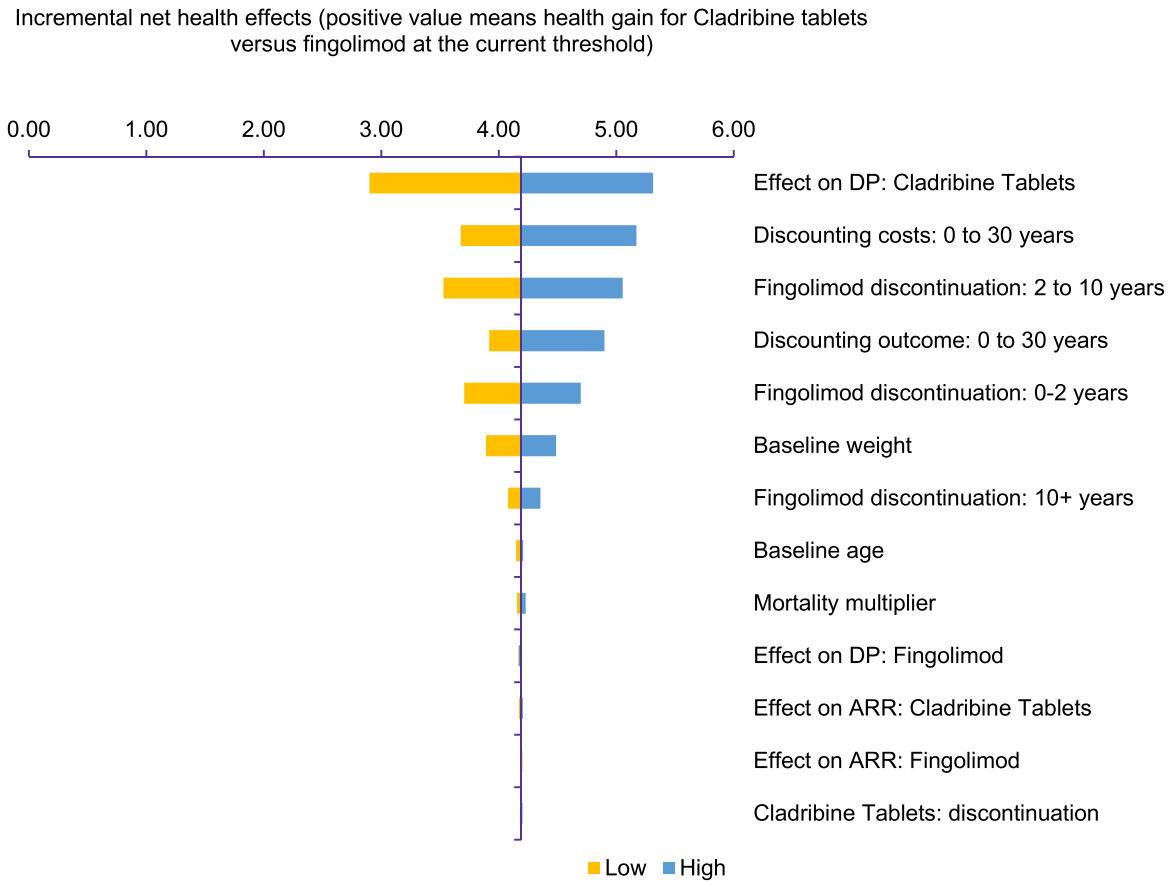

Fig. 1. Tornado diagram showing the drivers of cost-effectiveness for cladribine tablets versus fingolimod.

Table 3
Breakdown of total drug and non-drug cost for Scenario 1 (partial displacement) and Scenario 2 (100% displacement) in the budget impact analysis.

Cost (USD)s	Scenario 1 (partial displacement)				Scenario 2 (100% displacement)			
	Without cladribine tablets scenario	With cladribine tablets scenario	Incremental cost	% Incremental cost	Without cladribine tablets scenario	With cladribine tablets scenario	Incremental cost	% Incremental cost
Acquisition cost	23,519,464	22,571,242	-948,222	-4.0%	23,519,464	18,885,150	-4,634,314	-19.7%
Relapse cost	424,743	409,515	-15,228	-3.6%	424,743	389,620	-35,123	-8.3%
Administration cost	159,803	92,425	-67,378	-42.2%	159,803	0	-159,803	-100.0%
Monitoring cost	267,449	196,695	-70,754	-26.5%	267,449	101,437	-166,012	-62.1%
AE[a] management cost	1,274,413	1,087,288	-187,125	-14.7%	1,274,413	762,214	-512,199	-40.2%
Total budget impact	25,645,872	24,357,165	-1,288,707	-5.0%	25,645,872	20,138,423	-5,507,449	-21.5%

[a] AE; adverse event.

respectively. Therefore, treatment with cladribine tablets were considered a budget saving treatment strategy among HDA-RMS patients from Lebanon NSSF perspective.

There are some limitations regarding the analyses conducted. Major limitations include the requirement to assume no further DMD treatment after cessation of therapy, the dependence on NMA for efficacy and safety data from clinical trials that differ in many aspects such as study design, population characteristics, time frame over which data were collected, and the uncertainty surrounding the long-term efficacy of all DMDs. All base case analyses performed are subject to limitation owing to the limited availability of 6-month confirmed disability progression data for comparator therapies. However, a sensitivity analysis was run to alleviate the limitation, and multiple comprehensive further work and analysis were conducted with consistent results (Berardi et al., 2019) aligned with UK NICE base case (National Institute for Health and Care Excellence NICE, 2019). The efficacy comparison of all DMDs in the model were estimated from NMA considering 6-month CDP. There is a lack of head-to-head trials comparing the efficacy of DMDs, hence, the use of sub-set data (i.e. HDA-RMS) was required for the NMA. Also, the intention-to-treat population of the CLARITY studies consisted of relapsing-remitting multiple sclerosis (RRMS) patients and was not restricted to patients with HDA-RMS. The generalizability of this subgroup analysis data to the full HDA-RMS is not known, and is, therefore, a source of bias in the analysis. The analysis considers the cost-utility of cladribine tablets versus the comparators available in Lebanon at the time of the study.

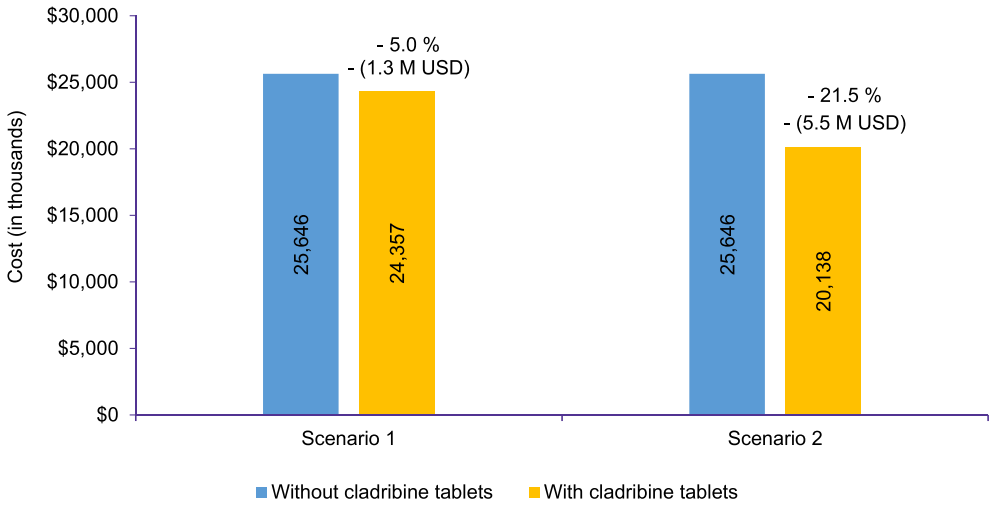

Fig. 2. Total Budget Impact for five years [Scenario 1 (partial displacement) and Scenario 2 (100% displacement)].

Table 4
Results for probabilistic sensitivity analysis.

Intervention	Mean Costs (USD)	95% CI[a] (costs) Lower bound	Upper bound	Mean QALY	95% CI (QALYs[b]) Lower bound	Upper bound	Mean costs	Mean QALY	ICER[c] vs. Cladribine tablets (QALY)	Probability CE[d] at USD 22,000
Cladribine tablets	233,276	222,307	243,803	7.308	4.911	9.716	Reference			
Alemtuzumab	271,581	263,304	280,057	7.082	4.558	9.548	-37,853	0.283	Cladribine dominant	99.3%
Fingolimod	303,082	281,245	324,674	6.302	4.204	8.490	-69,805	1.005	Cladribine dominant	100%
Natalizumab	301,946	268,348	341,813	6.763	4.584	8.859	-68,655	0.646	Cladribine dominant	100%

[a] CI; confidence interval.
[b] QALY; quality-adjusted life year.
[c] ICER; incremental cost-effectiveness ratio.
[d] CE; certainty equivalence.

In conclusion, according to the cost-utility analysis, cladribine tablets are an economically dominant therapeutic strategy when compared to alemtuzumab, fingolimod, and natalizumab, at a threshold of 22,000 USD per QALY gained which is mainly driven by drug acquisition, administration, and monitoring costs. Similarly, the budget impact analysis demonstrated that, in different scenarios, the introduction of cladribine tablets would likely lead to a reduction in the NSSF's budget ranging from 5% to 21.5%. Total displacement of DMDs by cladribine tablets proves to be more cost saving compared to partial displacement. These findings provide a useful summary of the economic implications of introducing cladribine tablets compared to other DMDs in the treatment of HDA-RMS patients in Lebanon. This study could act as evidence for policy makers, budget holders and health advisors to build informed decisions for the treatment coverage in Lebanon.

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CRediT authorship contribution statement

Mirna Matni: Validation, Supervision, Writing – review & editing. **Bassem Yamout:** Writing – review & editing, Validation, Supervision. **Salam Koussa:** Writing – review & editing, Validation, Supervision. **Chaker Khamis:** Writing – review & editing, Validation, Supervision. **Lora Fleifel:** Writing – review & editing, Conceptualization. **Shahdak Sharifi:** Writing – review & editing, Conceptualization. **Omneya Mohamed:** Writing – original draft, Writing – review & editing, Methodology.

Declaration of Competing Interest

Lora Fleifel and Shahdak Sharifi are both employees of Merck Serono Middle East FZ-Ltd, an affiliate of Merck KGaA, Darmstadt, Germany. Bassem Yamout has received research grants, honoraria for presentations and lectures, support for travel to scientific meetings; from Merck. Omneya Mohamed is a full-time paid employee of IQVIA who was paid as a third-party consultancy by Merck to conduct the economic evaluation and develop the manuscript. Mirna Matni, Salam Koussa, and Chaker Khamis declare they have no conflicts of interest.

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Supplementary materials

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