Cost-effectiveness Analysis of Dimethyl Fumarate in the Treatment of Relapsing-Remitting Multiple Sclerosis in Italy

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LG Mantovani[1], G Furneri[2], PA Cortesi[1], E Robberto[3], L Santoni[3], L Prosperini[4]

[1]Research Centre on Public Health (CESP), University of Milan – Bicocca, Milan, Italy; [2]EBMA Consulting, Health Economics, Pricing & Market Access Department, Melegnano (MI), Italy; [3]Biogen Italia, Milan, Italy; [4]Dept. of Neurosciences, S. Camillo-Forlanini Hospital, Rome, Italy

Conclusions

- The results of this cost-effectiveness analysis confirm that dimethyl fumarate (DMF) may be an optimal first-line treatment for Relapsing-Remitting Multiple Sclerosis in both Italian National Healthcare Service (NHS) and societal perspectives
- DMF is cost-effective vs teriflunomide, from the Italian NHS perspective, with an ICER value significantly below the Italian willingness-to-pay threshold considered (€ 50,000 per QALY)
- DMF is dominant vs teriflunomide, from the societal perspective, because it is more effective in terms of QALYs and less costly

Introduction

- Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system that results in progressive disability[1]
- MS affects approximately 2.3 million people worldwide, including 600,000 in Europe[2] and 118,000 in Italy (estimated incidence of 3,400 cases/year[3])
- Reduced work capacity, due to disease onset during working age, disease chronicity and progression of disease severity heavily impact societal costs and patients' quality of life[4]
- The annual cost of MS in Italy is estimated at € 5 billion[3]
- Delayed-release dimethyl fumarate (also known as gastro-resistant dimethyl fumarate, DMF) is an oral disease-modifying therapy used for the treatment of Relapsing-Remitting Multiple Sclerosis (RRMS)

Objectives

The aim of this economic analysis is to evaluate the cost effectiveness of DMF compared with teriflunomide in first-line treatment of RRMS in Italy, adopting both National Healthcare Service (NHS) and societal perspectives

Methods

Study design

- This cost-effectiveness analysis was conducted adapting a previously validated Markov model[5] for the Italian environment (Figure 1)
- The clinical and economic consequences of treating the study population with either DMF or teriflunomide were estimated
- Health outcomes and costs were evaluated over a 50-year time horizon (lifetime horizon). Both health outcomes and costs were discounted at 3.5%
- Outcomes were measured in terms of life years (LYs), quality-adjusted life years (QALYs), lifetime costs and incremental cost-effectiveness ratio (ICER)
- Data on the natural history of MS were considered and retrieved from published literature

Clinical and quality of life data

- The study population is a hypothetical cohort of Italian RRMS patients eligible to first line DMTs. Patients' clinical characteristics at baseline (age, gender, EDSS score) were derived from DMF clinical trials[6, 7]
- Efficacy of treatments (Table 1), expressed as reduction of disability progression and relapse rate, was derived from a mixed treatment comparison[8]
- Utilities were retrieved from the DMF clinical trials[6, 7] as well as from a survey conducted in the United Kingdom[9]. Relapses, adverse events, progression to secondary progressive MS (SPMS) were associated with disutilities

Economic data

- According to the Italian NHS and societal perspectives, in this economic analysis both direct and indirect costs were captured:
  - Pharmacological treatment acquisition (Table 2)
  - Administration
  - Treatment monitoring
  - Relapse management
  - Direct and indirect costs associated with disability
  - Adverse event management
- Administration costs were assumed equal to €0, because both DMF and teriflunomide are oral and self-administered
- Unit costs were based on current Italian prices, tariffs[10], published literature[11], and expresses in euros 2019

Sensitivity analyses

- One-way deterministic (OWSA) and probabilistic (PSA) sensitivity analyses were conducted, a cost-effectiveness acceptability curve (CEAC) was generated

Results

Base-case (Table 3)

DMF is more effective than teriflunomide for both LYs (19.63 vs. 19.55) and QALYs (6.53 vs. 5.95)

- *From Italian NHS perspective:*
  - Total costs per patient treated with DMF (€ 348,216) are slightly higher than with teriflunomide (€ 336,896)
  - Resulting ICER is € 19,741 per QALY gained, significantly below the Italian willingness-to-pay (WTP) threshold considered (€ 50,000 per QALY)
- *From societal perspective:*
  - Total costs per patient treated with DMF (€ 1.01 M) are lower than with teriflunomide (€ 1.03 M)
  - DMF is dominant because it is more effective in terms of QALYs and less costly

Sensitivity analyses

- Both OWSA and PSA confirm the robustness and reliability of base-case results
- The CEAC analysis shows that, using a WTP threshold of €50,000/QALY, the probability of DMF to be cost-effective vs. teriflunomide is 67.3% and 78.5% of simulations respectively from Italian NHS (Figure 2) and societal perspectives (Figure 3). Moreover, DMF dominates teriflunomide in the 72.2% of the simulations from the societal perspective (Figure 3)

Figure 1. Scheme of the Markov model[5]

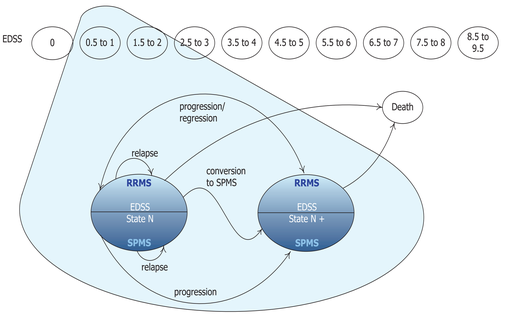

Figure 2. Results of probabilistic sensitivity analysis in NHS perspective

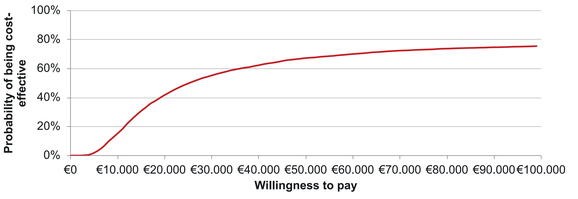

Figure 3. Results of probabilistic sensitivity analysis in societal perspective

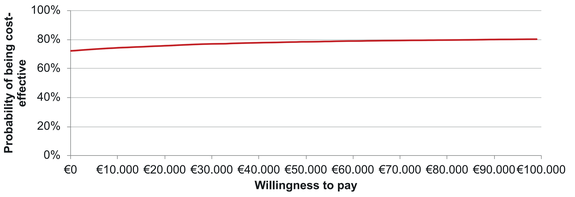

Table 1. Effects of treatments vs. placebo[7]

Treatment	ARR RR vs. placebo (CI 95%)	CPDS3M HR vs. placebo (CI 95%)
DMF 240 mg, twice daily	0.5269 (0.4507-0.6159)	0.6051 (0.4713-0.7767)
Teriflunomide 14 mg, daily	0.7113 (0.6224-0.8129)	0.7106 (0.5736-0.8803)
Placebo	Reference	Reference

ARR = annualized relapse rate; RR = risk ratio; CPDS3M = confirmed progression of disability sustained for 3 months; HR = hazard ratio; CI = confidence interval

Table 2. Pharmacological treatment acquisition costs

Treatment and posology	Ex -factory price* (1 pack)	Source
DMF 240 mg, twice daily	1,153.00 (56 capsules, 240 mg)	Official Journal 19 2015 [12]
Teriflunomide 14 mg, daily	1,027.75 (28 tablets, 14 mg)	Official Journal 187 2014 [13]

*Not including temporary law reductions and any hidden discount applied to public structures of Italian NHS

Table 3. Base-case: results of the cost-effectiveness analysis

Item	DMF	Teriflunomide	Difference
Per-patient outcomes			
Life Years (LYs)	19.63	19.55	0.08
QALYs	6.53	5.95	0.58
Per-patient total costs (€) from NHS perspective and ICER			
Total costs	348,216	336,896	11.320
ICER (€/QALY) DMF vs teriflunomide	**€19,741**		
Per-patient total costs (€) from societal perspective and ICER			
Total costs	1,008,345	1.028.579	-20,234
ICER (€/QALY) DMF vs teriflunomide	**Dimethyl fumarate is dominant**		

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