Cost-effectiveness of Fingolimod, Teriflunomide, Dimethyl Fumarate and Intramuscular Interferon Beta-1a in Relapsing-remitting Multiple Sclerosis

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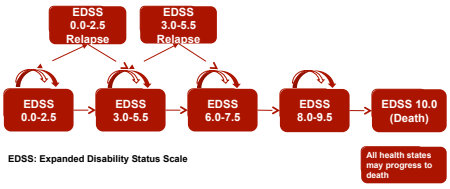
Objective

To compare the cost-effectiveness of fingolimod, teriflunomide, dimethyl fumarate and IM IFN β-1a as first-line therapies in treatment of patients with relapsing-remitting multiple sclerosis (RRMS).

Methods

- A Markov model was developed to evaluate the cost-effectiveness of disease-modifying drugs from a US societal perspective. Time horizon in base case was 5 years [Figure 1].
- Model parameters were obtained from randomized controlled trials, natural history studies of multiple sclerosis, cross-sectional surveys and federal supply schedule drug prices [Table 1].
- Outcomes included quality-adjusted life years (QALYs), incremental net monetary benefit (INMB) and incremental cost-effectiveness ratio (ICER). The societal willingness-to-pay (WTP) threshold was assumed to be $100,000 per QALY.
- Costs were reported in 2012 US dollars and both costs and outcomes were discounted at 3% annual rate in base case.
- One-way sensitivity analyses and probabilistic sensitivity analyses were conducted to test the robustness of the model results.

Figure 1. Markov model for disease progression of MS



EDSS: Expanded Disability Status Scale

Table 1. Parameters and range in one-way sensitivity analysis

Parameters	Base Case	One-way SA Range		sources
Monthly probability of disease progression (SM)				
EDSS 0.0-2.5	0.005760			1
EDSS 3.0-5.5	0.007194	N/A		1
EDSS 6.0-7.5	0.005760			1
Monthly probability of progressing to death				
EDSS 0.0-2.5	0.001684			2
EDSS 3.0-5.5	0.002248	N/A		2
EDSS 6.0-7.5	0.003121			2
EDSS 8.0-9.5	0.004457			2
Annual relapse rate for SM	0.400	N/A		3
Annual relapse rate for FIN	0.160	0.128	0.192	4
Annual relapse rate for IM IFNβ-1a	0.330	0.264	0.396	4
HR of disease progression				
FIN vs. SM	0.700	0.560	0.840	3
IM IFNβ-1a vs. FIN	1.353	1.083	1.624	4
TER vs. SM	0.700	0.560	0.840	5
DF vs. SM	0.620	0.496	0.744	6
NAT vs. SM	0.580	N/A		7
HR of annual relapse rate				
TER vs. SM	0.720	0.576	0.864	5
DF vs. SM	0.510	0.408	0.612	6
NAT vs. SM	0.410	N/A		7
Annual discontinuation rate for FIN	0.103	0.082	0.123	4
Annual discontinuation rate for IM IFNβ-1a	0.118	0.095	0.142	4
Discontinuation rate for TER, 2yr	0.265	0.212	0.318	5
Discontinuation rate for DF, 2yr	0.310	0.248	0.372	6
Discontinuation rate for NAT, 2yr	0.083	N/A		7
Assignment ratio between NAT and SM	0.5:0.5	0 : 1	1 : 0	
Utilities estimates				
Utility EDSS 0.0-0.2.5	0.899	0.719	1	8
Utility EDSS 3.0-0-5.5	0.821	0.657	1	8
Utility EDSS 6.0-0-7.5	0.769	0.615	0.923	8
Utility EDSS 8.0-0-9.5	0.491	0.393	0.589	8
Disutility for Relapse	-0.094	-0.075	-0.113	9
Disutility for IM IFNβ-1a	-0.115	-0.092	-0.138	8
Impact of FIN on utility	0	-0.03	0.03	10,11
Impact of TER on utility	0	-0.03	0.03	12
Impact of DF on utility	0.01	-0.03	0.03	13
Impact of NAT on utility	0	N/A		14
Monthly costs, 2012 US dollar				
WAC for FIN	$4,164	$ 3,331	$ 4,996	15
WAC for IM IFNβ-1a	$3,835	$ 3,068	$ 4,602	15
WAC for NAT	$3,320	$ 2,656	$ 3,984	15
WAC for TER	$3,704	$ 2,963	$ 4,444	15
WAC for DF	$3,346	$ 2,676	$ 4,015	15
Cost of EDSS 0.0-2.5	$1,730	$ 1,384	$ 2,076	9
Cost of EDSS 3.0-5.5	$3,691	$ 2,953	$ 4,430	9
Cost of EDSS 6.0-7.5	$5,395	$ 4,316	$ 6,475	9
Cost of EDSS 8.0-9.5	$10,791	$ 8,633	$12,949	9
Cost of relapse	$5,008	$ 4,006	$ 6,009	16
Discount Rate	0.03	0	0.05	
Time Horizon	5 years	2 years	10 years	

SM: Symptom management; FIN: Fingolimod; TER: Teriflunomide; DF: Dimethyl fumarate; NAT: Natalizumab; WAC: Wholesale average cost
* ±20% unless indicated

Results

Base case

- The 5 years' total costs per patient were estimated at $322,694, $339,457, $324,512 and $298,875 for IM IFN β-1a, fingolimod, teriflunomide, and dimethyl fumarate, respectively. The accumulated QALYs associated with each drug were 3.34, 3.69, 3.68 and 3.72, respectively [Table 2].
- Compared with IM IFN β-1a, at the WTP of $100,000, INMBs were estimated at $18,510, $33,021, and $61,290 for fingolimod, teriflunomide, and dimethyl fumarate, respectively. Compared with IM IFN β-1a, ICERs were $47,523 and $5,218 for fingolimod and teriflunomide, respectively [Table 2].
- Dimethyl fumarate dominated all other drugs over the range of WTPs from $0 to $180,000 [Figure 2].

Sensitivity analysis

- One-way sensitivity analyses found model results were robust to most parameter variations. When the monthly cost of fingolimod was beyond $4,654 or the monthly cost of IM IFN β-1a was below $3,304, then fingolimod would no longer be cost-effective compared with IM IFN β-1a [Figure 3]. Other one-way sensitivity analysis comparison figures are available on request.
- Probabilistic sensitivity analysis showed that for more than 90% of the simulations, dimethyl fumarate was the optimal therapy across all willingness-to-pay values [Figure 4].

Table 2. Base case results, compared with IM IFN β-1a (WTP=$100,000)

	Cost	QALY	NMB	INMB vs. IM IFN β-1a	CER	ICER vs. IM IFN β-1a
IM IFN β-1a	$322,694	3.34	$10,873		$96,741	
Fingolimod	$339,457	3.69	$29,382	$18,510	$92,034	$47,523
~~**Teriflunomide**~~	~~$324,512~~	~~3.68~~	~~$43,894~~	~~$33,021~~	~~$88,085~~	$5,218
Dimethyl fumarate	$298,875	3.72	$72,792	$61,920	$80,415	Dominant

Figure 2. Incremental net monetary benefit of oral drugs vs IM IFN β-1a

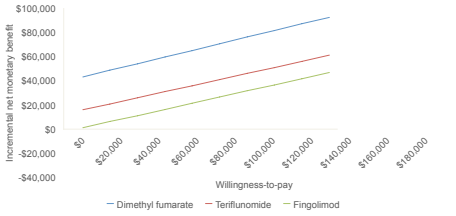


Figure 3. One-way sensitivity analysis

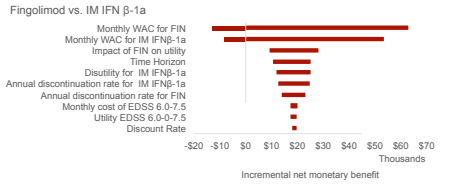
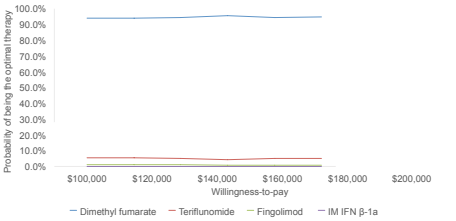


Figure 4. Probability that each therapy maximizes net monetary benefit



Conclusion

The oral therapies were favored in the cost-effectiveness analysis. Of the four disease-modifying drugs, dimethyl fumarate was the dominant therapy to manage RRMS. Apart from dimethyl fumarate, teriflunomide was the most cost effective therapy compared with IM IFN beta-1a.

Key References

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