

Cost-Effectiveness of Cladribine Tablets and Dimethyl Fumarate in the Treatment of Relapsing Remitting Multiple Sclerosis in Spain

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CONCLUSION

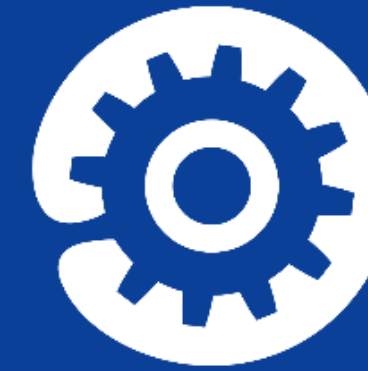


CladT had a 95.1% probability of being cost-effective for a willingness to pay of €25,000 per QALY gained compared with DMF in the treatment of RRMS in Spain.

CladT was also the dominant treatment (lower costs, with more QALYs) across all scenarios tested.



The QALYs gain (0.1920) with CladT vs DMF was clinically relevant since it is generally considered that the minimum clinically relevant utility difference between two interventions would be between 0.030 and 0.074 QALYs .



The use of CladT could be an efficient management strategy that generates savings and therefore contributes to the sustainability of the NHS in Spain



INTRODUCTION

- In an economic study published in the Spanish Health Economic Association annual meeting, spending in disease-modifying therapies (DMTs) for Multiple Sclerosis (MS) has increased in the last years mainly due to the incorporation of innovative therapies (1).
- Economic modelling can provide useful information to help decision-makers make informed evaluations on the efficient management strategy that generates savings and therefore contributes to the sustainability of the NHS in Spain.



OBJECTIVE

- To analyse the cost-effectiveness of treatment of relapsing remitting multiple sclerosis (RRMS) with cladribine tablets (CladT) and dimethyl fumarate (DMF) from the perspective of the National Health System (NHS) in Spain.



METHODS

- A probabilistic Markov model (second-order Monte Carlo simulation) with a 10-year time horizon and annual Markov cycles was performed, based on a model developed by the Canadian Agency for Drugs and Technologies in Health (CADTH) (2) (Figure 1).
- Data on progression, relapses, treatment adherence, treatment continuation and utilities (quality-adjusted life years [QALYs]) were obtained from the medical literature (2-5).
- The cost of drugs, monitoring, EDSS status, relapses, and adverse reactions were obtained from Spanish sources (6-9) (Table 1). All unit costs were updated to the year 2021 using the consumer price index (CPI) of the National Institute of Statistics.

Figure 1. 5-state Markov model.

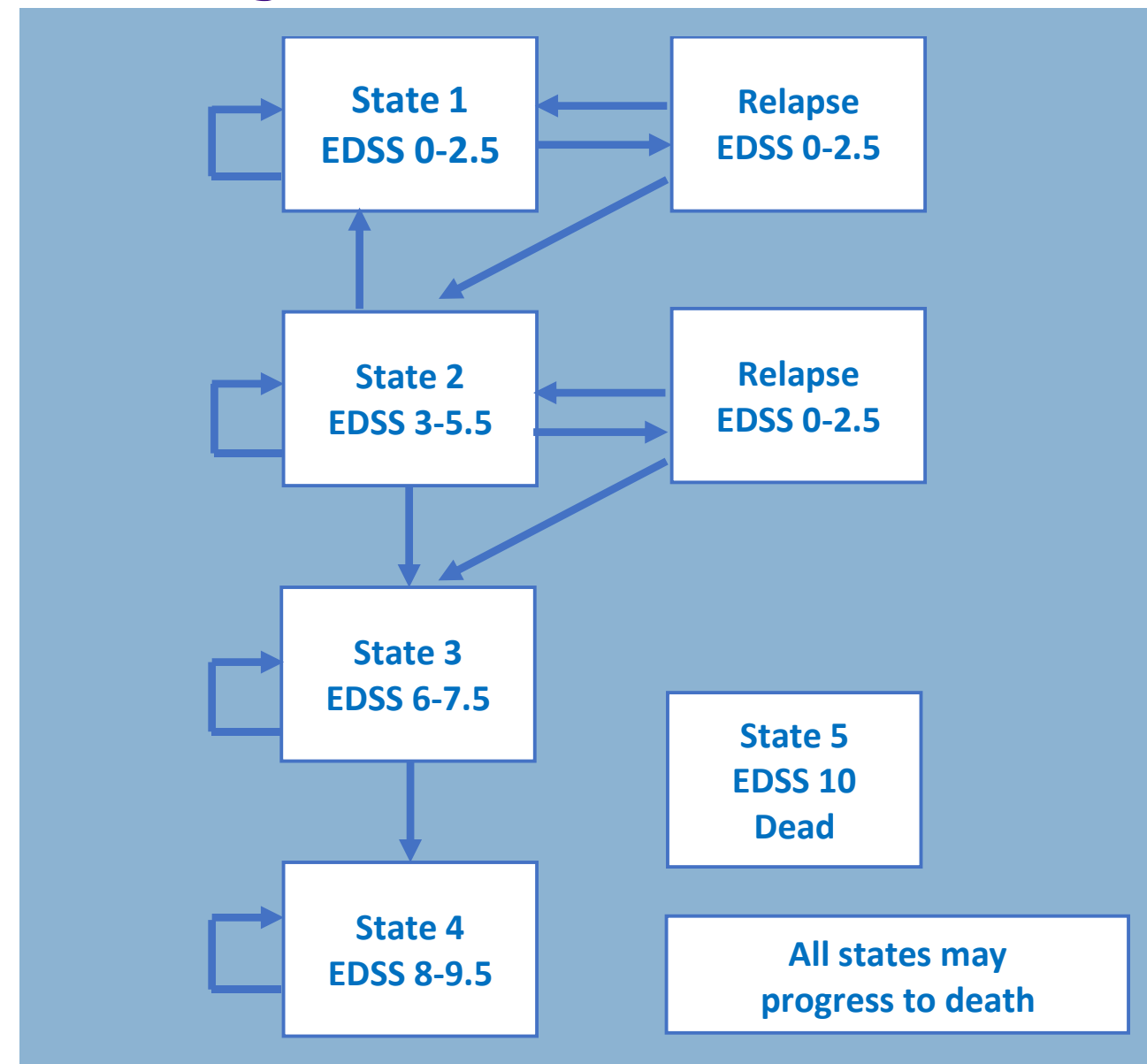


Table 1. Unit costs.

Cost per patient / event	CladT	DMF
Drug treatment (10 years)	92,151 €	153,300 €
Monitoring (1 year)	121.95 €	317.20 €
Adverse reactions (1 year)	852.15 €	862.24 €
State 1	3,500 €	
State 2	11,567 €	
State 3	22,933 €	
State 4	43,246 €	
Relapse	7,966 €	

- Univariate sensitivity analyses (modifying time horizon, cost of treatment continuation, and CladT and DMF purchase prices) were performed to confirm and provide robustness to the results.



RESULTS

- CladT was the dominant treatment with lower costs (-74,741 € [95% CI -67,247; -85,661 €]) (Figure 2) and greater effectiveness (0.1920 [95% CI -0.1659; 0.2173] QALY) per patient, compared to DMF (Figure 3).

Figure 2. Cost difference per patient

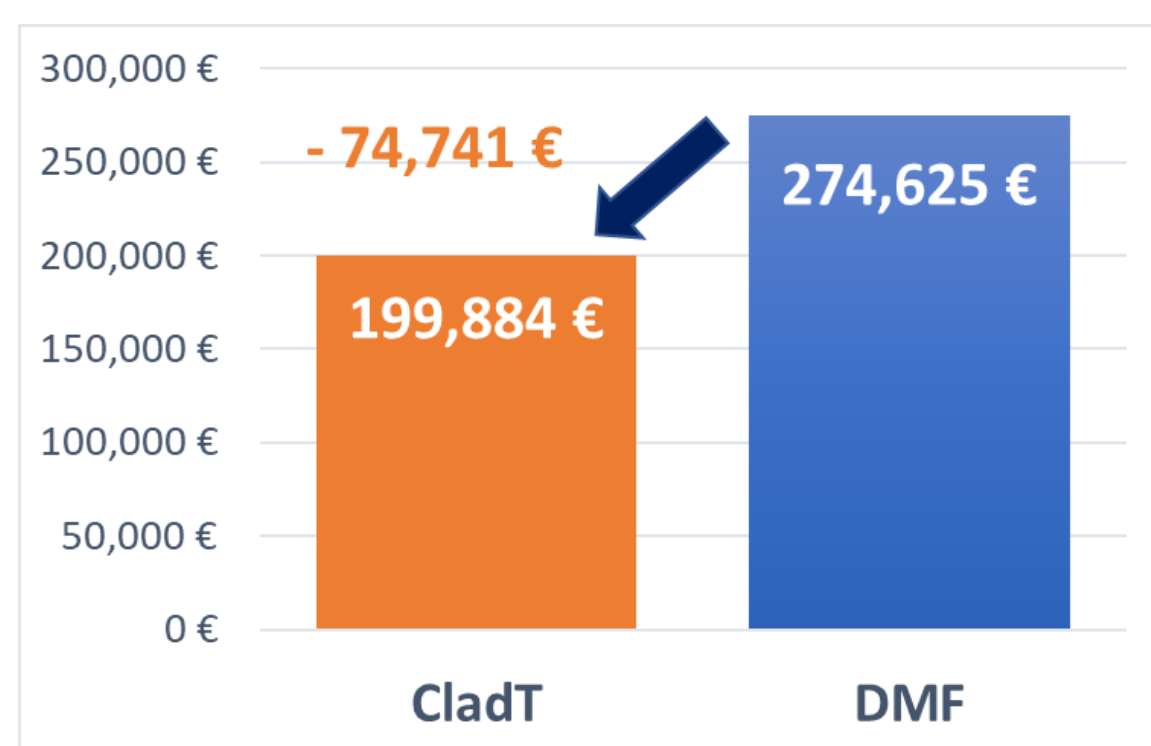
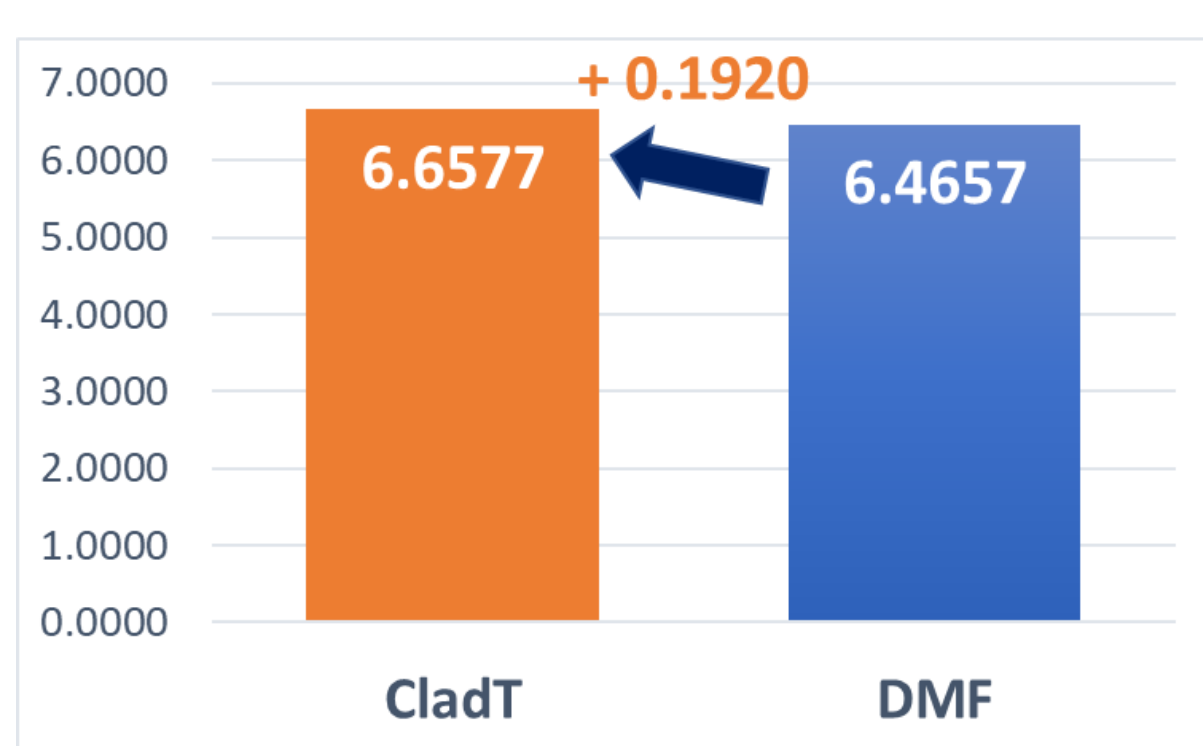


Figure 3. QALY difference per patient



- The use of CadT versus DMF had a 95.1% probability of being cost-effective for the NHS in a 10-year time horizon assuming a willingness to pay of 25.000 euros per QALY gained (Table 2, Figure 4) and remained dominant in 94.1% of the analyses. The sensitivity analyses confirmed the results (Figure 5).

Table 2. Base case results

Treatment	Total cost per patient, mean (95% CI)	QALY per patient, mean (95% CI)	Difference in costs	Difference in QALY	Probability of cost-effectiveness CladT vs DMF
CladT	199,884 € (174,395; 229,860 €)	6.6577 (2.4954; 7.4436)	-74,741 € (-67,247; -85,661 €)	0.1920 (-0.1659; 0.2173)	95.1%
DMF	274,625 € (241,642; 315,521 €)	6.4657 (2.6613; 7.2263)			

- The QALY gain (0.1920) with CladT vs DMF was clinically relevant, which means beneficial to the patient (10).
- Both, the effect of CladT on disability progression derived from the indirect treatment comparison (3) along with the savings in costs due to the CladT posology had a significant influence on the results.

Figure 4. Cost-effectiveness plane

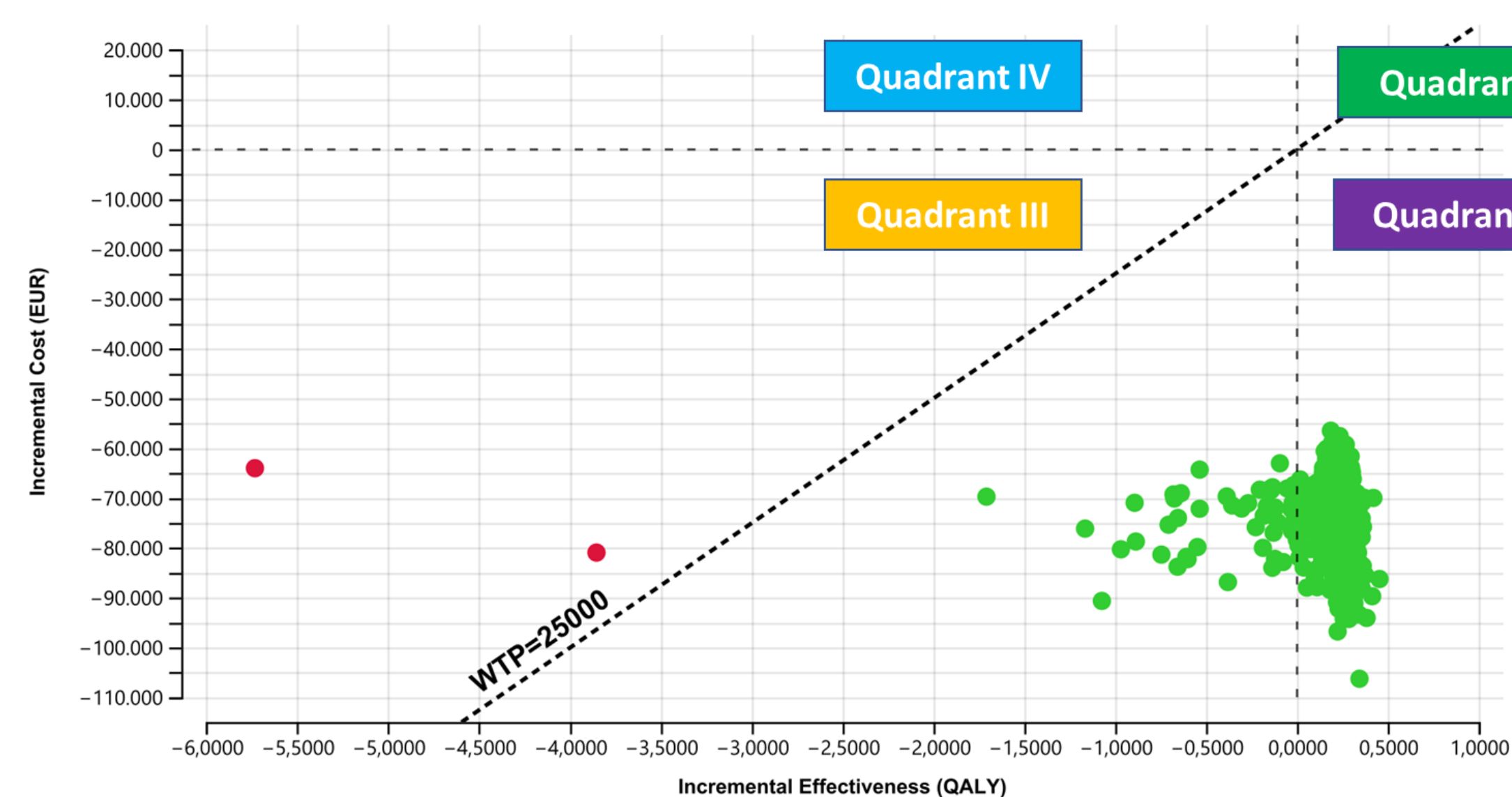
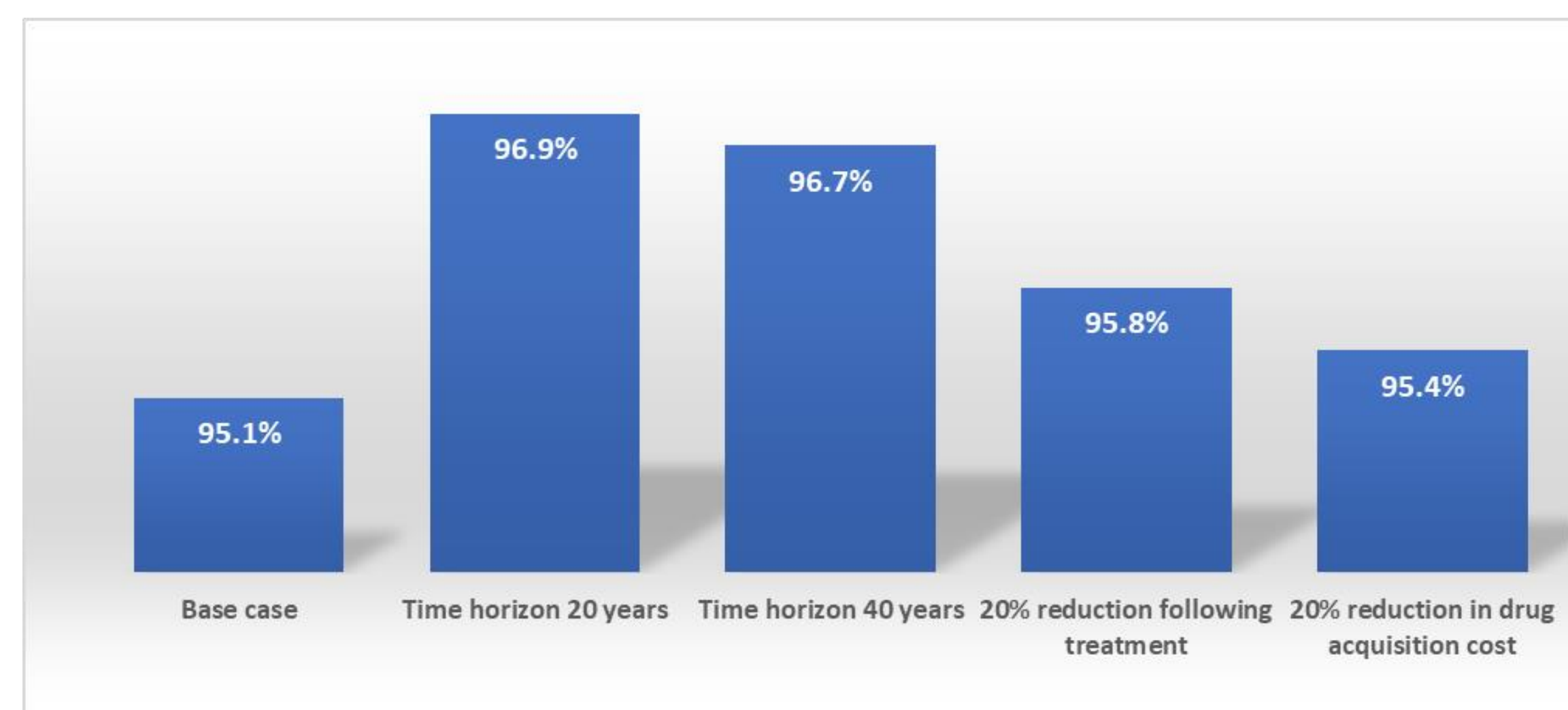


Figure 5. Probability that CladT is cost-effective vs DMF



1. Hidalgo A, Ivanova N, Nozaya N. Análisis del gasto asociado a los tratamientos de esclerosis múltiple en España durante el periodo 2004-2016. Available from: https://www.aes.es/Jornadas2017/pdfs/posters/Aes_2017_14_1.pdf (Accessed on: 06/06/2022).
2. Canadian Agency for Drugs and Technologies in Health. CADTH therapeutic review. Comparative clinical and cost-effectiveness of drug therapies for relapsing-remitting multiple sclerosis [Internet]. Ottawa: The Agency; 2013 Oct. (CADTH Therapeutic Review vol.1, no. 2b). Available from: http://www.cadth.ca/media/pdf/TR0004_RRMS_ScienceReport_e.pdf.
3. Siddiqui MK, Khurana TS, Budhia S, et al. Systematic literature review and network meta-analysis of cladribine tablets versus alternative disease-modifying treatments for relapsing-remitting multiple sclerosis. Curr Med Res Opin. 2017; 34: 1361-71.
4. Su W, Kansal A, Vicente C, Diaz S, Sarda S. The cost-effectiveness of delayed-release dimethyl fumarate for the treatment of relapsing-remitting multiple sclerosis in Canada. J Med Econ. 2016; 19: 718-27.
5. Signori A, Sacà F, Lanzillo R, Maniscalco GT, Signoriello E, Repice AM. Cladribine vs other drugs in MS: Merging randomized trial with real-life data. Neurol Neuroimmunol Neuroinflamm. 2020; 7: e878.
6. Casado V, Martínez-Yélanos S, Martínez-Yélanos A, Carmona O, Alonso L, Romero L, Moral E, Gubieras L, Arbizu T. Direct and indirect costs of Multiple Sclerosis in Baix Llobregat (Catalonia, Spain), according to disability. BMC Health Serv Res. 2006; 6: 143.
7. Casado V, Bonaventura I, Bieva L, Martínez-Yélanos S, Martín G, Perras-Rodríguez S, et al. Direct costs of relapses in patients with Relapsing-remitting Multiple Sclerosis. Neurol Persp. 2021; DOI: <https://doi.org/10.1016/j.neurop.2021.05.003>.
8. Poveda JL, Trillo JL, Rubio-Terrés C, Rubio-Rodríguez D, Polanco A, Torres C. Cost-effectiveness of Cladribine Tablets and fingolimod in the treatment of relapsing multiple sclerosis with high disease activity in Spain. Expert Rev Pharmacoecon Outcomes Res. 2020; 20: 295-303.
9. BotPlus 2.0. Consejo General de Colegios Oficiales de Farmacéuticos (CGCOF). 2021. Available at URL: www.portalfarma.com (Accessed on: 18/06/2021).
10. Wee H-L, Machin D, Loke W-C, Li S-C, Cheung Y-B, Luo N, et al. Assessing differences in utility scores: a comparison of four widely used preference-based instruments. Value Health. 2007; 10: 256-65.

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