A Cost-effectiveness Analysis Using Real-World Data From the MSBase Registry: Comparing Natalizumab to Fingolimod in Patients With Inadequate Response to Disease-Modifying Therapies in Relapsing-Remitting Multiple Sclerosis in Italy

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Conclusions

- Switching to natalizumab (NTZ) dominated switching to fingolimod (FTY) (lower costs and better health outcomes) in the base-case cost-effectiveness analysis utilizing real-world (RW) comparative effectiveness data from the MSBase Registry for patients with highly active relapsing-remitting multiple sclerosis (HA-RRMS) with inadequate response to first-line disease-modifying therapies in Italy.
- NTZ remained dominant or cost-effective compared with FTY at a willingness-to-pay (WTP) threshold of €30,000 per quality-adjusted life-year (QALY) gained for one-way and probabilistic sensitivity analyses and across a range of alternative scenarios.

Background

- Patients with HA-RRMS in Italy who experience disease activity with first-line disease-modifying therapies (collectively, BRACE-TD) may consider therapy escalation to NTZ or FTY.[1,2]
- The international MSBase Registry includes long-term, observational data that have been used to generate evidence of the RW effectiveness of escalation to NTZ and FTY in patients with HA-RRMS.[3]

Objective

- To estimate the cost-effectiveness of switching to NTZ compared with switching to FTY in patients with HA-RRMS with inadequate response to first-line BRACE-TD from a societal perspective in Italy using RW comparative effectiveness results from MSBase.

Methods

Population

- The target population included adult patients with HA-RRMS who have completed at least 1 year of BRACE-TD therapy and have experienced at least 1 relapse in the previous year.

Modeling Approach

- A previously presented, Markov-based cohort model with Expanded Disability Status Scale (EDSS) health states tracking disability, conversion to secondary progressive MS (SPMS), and relapses over time[4] was adapted to Italy.
- A lifetime horizon was considered using a 1-year cycle length. Costs and outcomes were discounted at a rate of 3.5% per year. All costs were inflated to 2017 currency levels.

Clinical Input Parameters

- The primary clinical data used to populate the model, including the MSBase analysis methodology and results, have been presented previously (Table 1).[3,4]

Cost and Utility Input Parameters

- The following treatment-specific cost and utility data were used in the model (Table 1):
  - Acquisition, administration, and monitoring costs for NTZ and FTY were obtained from publicly available national and regional data sources in Italy[5-7] and supplemented with expert clinical opinion.
  - Weighted average costs and utility decrements for adverse events (AEs), including fatal and nonfatal progressive multifocal leukoencephalopathy (PML) cases, were obtained from Italian tariffs for outpatient services, previous economic evaluations, published literature, other publicly available data, and assumptions.
- Direct and indirect costs and utility estimates were obtained from a recent MS burden-of-illness survey conducted in Italy and the United Kingdom, as shown in Table 2.[8-10]

Table 1. Treatment-Specific Input Parameters

	NTZ	FTY
Comparative effectiveness outcomes[a] (reference = switching to another BRACE-TD therapy)		
Mean (SD) years of follow-up	2.56 (1.71)	2.05 (1.27)
RR of relapse (95% CI)	0.64 (0.57, 0.72)*	0.91 (0.81, 1.03)
HR for 6-month-confirmed disability progression (95% CI)	1.01 (0.73, 1.40)	1.08 (0.78, 1.50)
HR for 6-month-confirmed disability regression (95% CI)	1.67 (1.30, 2.15)*	1.30 (0.99, 1.72)
Treatment discontinuation		
Discontinuation per year	6.3%	10.3%
Treatment costs per year		
Acquisition, administration, and monitoring (year 1; years 2+)	€21,399; €20,716	€18,973; €18,597
AE outcomes per year on treatment[b] (weighted average)		
Costs	€42.84	€28.60
Utility decrement	0.0057	0.0068

* $P < 0.001$.
CI = confidence interval; HR = hazard ratio; RR = relative risk; SD = standard deviation.
[a] Obtained from previous analyses.[3,4,10]
[b] AEs included were abdominal pain, abnormal liver-function test, alanine aminotransferase increase, aspartate aminotransferase increase, back pain, depression, diarrhea, fatigue, gastroenteritis, headache, infection, influenza-like illness, insomnia, nausea, paraesthesia, and PML.

Table 2. Costs and Utility Estimates by EDSS

	Direct Costs		Indirect Costs		Utility Values/Decrements	
EDSS Score	RRMS	SPMS	RRMS	SPMS	RRMS	SPMS
Disease Management	(annual cost)		(annual cost)		(utility values)	
0	€3,501	€4,316	€1,504	€1,853	0.908	0.888
1					0.797	0.777
2					0.705	0.685
3					0.583	0.563
4	€14,417	€17,772	€8,356	€10,300	0.615	0.595
5					0.579	0.559
6					0.490	0.470
7	€26,517	€32,687	€15,802	€19,479	0.407	0.387
8					0.167	0.147
9					−0.101	−0.121
Relapses	(cost per event)		(cost per event)		(utility decrement per event)	
0-3	€1,715		€737		0.013	
4-6	€1,552		€900			
7-9	€1,536		€916			

Sources: Battaglia et al., 2017[8]; Thompson et al., 2017[9]; Biogen data on file, 2017.[10]

Results

Base-Case Analysis

- As shown in Table 3, NTZ dominated FTY in the base-case analysis, leading to improved health outcomes and lower total costs.
  - Switching to NTZ resulted in increased QALYs and fewer lifetime relapses compared with switching to FTY.
  - Additional treatment-related costs associated with NTZ were offset by the reductions in direct and indirect MS-related costs.

Sensitivity and Scenario Analyses

- In one-way sensitivity analysis, NTZ remained dominant or cost-effective at a WTP threshold of €30,000/QALY gained compared with FTY for most of the parameters varied (Figure 1).
- In probabilistic sensitivity analysis (PSA), NTZ was dominant in 51.3% of simulations and had an 88.4% probability of being cost-effective at a WTP threshold of €30,000/QALY gained (Figure 2).
- In scenario analyses considering direct costs only, shorter time horizons, alternative discount rates, and equal treatment discontinuation rates, NTZ remained dominant or maintained an incremental cost-effectiveness ratio (ICER) less than €30,000/QALY gained except when a 10-year horizon was considered.
- NTZ remained dominant compared with FTY with a discount of up to 1.7% on the FTY net price and remained cost-effective at a WTP threshold of €30,000/QALY gained with up to a 23.0% reduction in the FTY net price.

Table 3. Base-Case Cost-effectiveness Analysis Outcomes

	NTZ	FTY	Incremental (%)
Expected health outcomes per patient			
Number of relapses (undiscounted)	14.04	15.07	−1.03 (−6.9%)
LYs	20.78	20.89	−0.11 (−0.5%)
QALYs	6.80	6.24	0.56 (9.0%)
Expected cost outcomes per patient			
Treatment-related costs	€120,509	€83,027	€37,482 (45.1%)
Direct MS-related costs	€460,104	€484,026	−€23,922 (−4.9%)
Indirect MS-related costs	€268,890	€283,751	−€14,860 (−5.2%)
Total costs	€849,503	€850,804	−€1,301 (−0.2%)
Incremental cost-effectiveness ratio			
Incremental cost per QALY gained	−€2,325 [NTZ dominates FTY]		

LY = life-year.

Figure 1. Tornado Diagram for One-Way Sensitivity Analysis

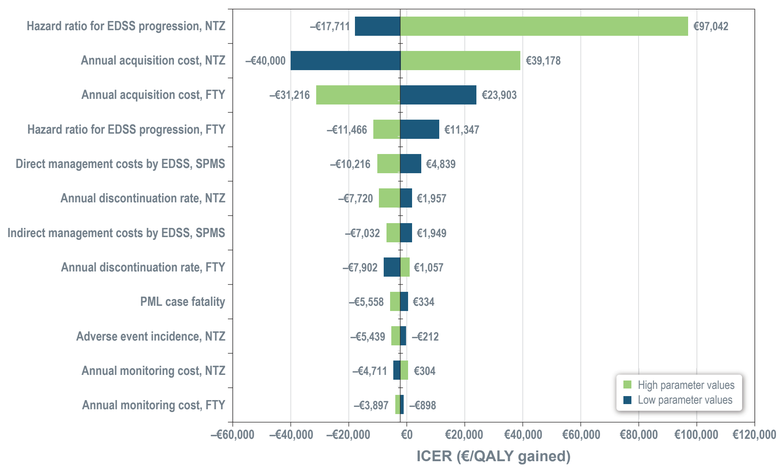
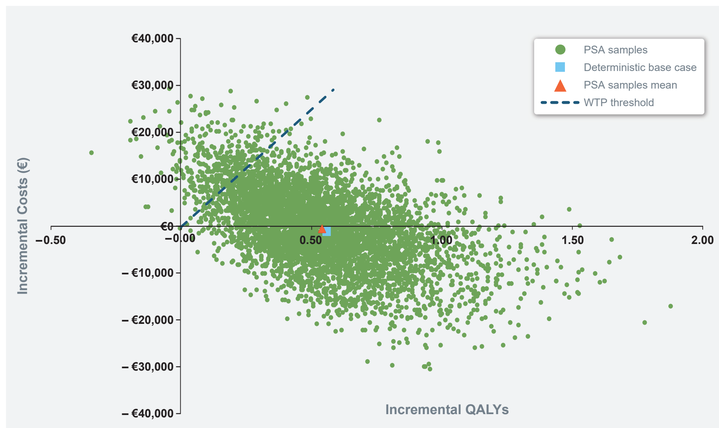


Figure 2. Cost-effectiveness Scatter Plot for Probabilistic Sensitivity Analysis



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