EE226

Productivity Loss Among Persons With Multiple Sclerosis Treated With Ocrelizumab vs Other Disease-Modifying Therapies

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BACKGROUND

- Multiple sclerosis (MS) is a chronic, demyelinating disease that can lead to permanent and worsening neurological disability and is frequently diagnosed at 20 to 40 years of age—during prime working years[1]
- Previous research has demonstrated that people with MS (pwMS) are less likely to be employed, have higher rates of absenteeism and have lower income compared with healthy controls[2]
- In addition, research has demonstrated that employment and work productivity decline with increasing levels of disability among pwMS[3]
- High-efficacy disease-modifying therapies (DMTs), such as ocrelizumab, can delay disease progression and improve long-term outcomes for pwMS, but data are lacking comparing productivity outcomes among pwMS treated with DMTs

OBJECTIVE

- To estimate long-term differences in employment status and reductions in market and nonmarket productivity among pwMS receiving ocrelizumab vs other DMTs

METHODS

General Model Settings

Table 1. Key Components of Model Framework

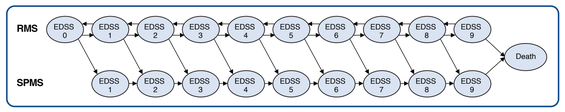
Model parameters	
Model structure	Markov model with 20 health states (based on CEA)[4,5]
Target population	Adults (18–55 years of age) with relapsing MS (OPERA I/II [NCT01247324/NCT01412333])[6]
Intervention	Ocrelizumab
Comparators	• Dimethyl fumarate (moderate efficacy) • Fingolimod (moderate efficacy) • Natalizumab (high efficacy) • Ofatumumab (high efficacy) • Ublituximab (high efficacy)
Time horizon	10 years
Time on treatment	• PwMS remained on treatment for the entire model time horizon; however, treatment switching was captured following initial treatment discontinuation • Trial-reported discontinuation rates (**Supplemental Table S1**) were annualized and applied over the first 2 years after initiating treatment • Discontinuation after 2 years was assumed to be related to serious adverse events only and did not vary by treatment
Productivity inputs	• Average wage • Average annual hours worked in general population • Employment rate by EDSS • Hours worked by EDSS • Health utility by EDSS
Model outcomes	• Market and nonmarket productivity (**Figure 2**) costs by comparator • Employment rates by comparator

CEA, cost-effectiveness analysis; EDSS, Expanded Disability Status Scale; MS, multiple sclerosis; pwMS, people with multiple sclerosis.

Model Structure

- In the Markov model (**Figure 1; Table 1**), pwMS transitioned between Expanded Disability Status Scale (EDSS) health states using transition probabilities derived in the absence of treatment with a DMT, consistent with published cost-effectiveness analyses (CEAs) in MS[4,5,7]
  - Treatment-specific effects for each intervention were applied to obtain DMT-specific transition probabilities for each comparator
  - Differences in disease worsening in the model were based on estimates of hazard ratios (HRs) for 6-month confirmed disability progression (CDP) obtained from an external network meta-analysis (NMA)[4,5]

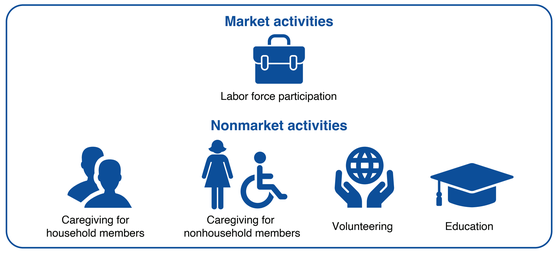
Figure 1. Markov Model EDSS Health States



EDSS, Expanded Disability Status Scale; RMS, relapsing multiple sclerosis; SPMS, secondary progressive multiple sclerosis.

Productivity Outcomes

Figure 2. Market and Nonmarket Activities



- Results from the North American Research Committee on MS work productivity survey were used to estimate market productivity losses by Patient-Determined Disease Steps (PDDS) score[3]
- The PDDS-based results were translated per a published crosswalk method[8] to align with the EDSS health states in published CEAs (**Table 2**)

Table 2. Model Inputs for Estimating Market Productivity Losses by EDSS Health State

EDSS	Employed, %	Average time worked per week, hours[a]	Annual work missed, days[a]
0	81.0	36.3	6.6
1	81.0	36.3	6.6
2	69.4	35.4	6.8
3	37.5	31.1	15.4
4	50.1	34.3	8.8
5	24.0	31.6	12.6
6	22.5	31.8	19.8
7	11.7	29.3	18.6
8	0	NA	NA
9	0	NA	NA

EDSS, Expanded Disability Status Scale; MS, multiple sclerosis; NA, not applicable.
[a]Only evaluated in the employed population.

- Data from the US Bureau of Labor Statistics reflecting the general US population were incorporated into the model
  - Hourly wage plus fringe benefits: $43.93
  - Average annual working time per worker: 1790 hours
  - Labor force participation rates by age (**Table 3**)

Table 3. Labor Force Participation Rates by Age

Age group, years	Labor force participation rate, %
35 to 44	83.0
45 to 54	81.1
55 to 64	65.2
65 to 74	26.6
≥75	8.2

- A published proxy productivity algorithm[9] was used to estimate nonmarket productivity losses by EDSS (**Table 4**)
  - The algorithm accounts for age as well as the health-related quality of life associated with each EDSS[5]

Table 4. Model Inputs for Estimating Nonmarket Productivity Losses by EDSS Health State

EDSS	RMS utility[a]	SPMS utility[a]
0	0.88	NA
1	0.83	0.79
2	0.78	0.74
3	0.69	0.65
4	0.63	0.58
5	0.54	0.50
6	0.46	0.41
7	0.34	0.30
8	0.24	0.21
9	0.13	0.10

EDSS, Expanded Disability Status Scale; NA, not applicable; RMS, relapsing multiple sclerosis; SPMS, secondary progressive multiple sclerosis.
[a]Utility values range from 0 (death) to 1 (perfect health).

- Per-patient model results were scaled to the population level using MS prevalence (124.97 per 100,000)[10]

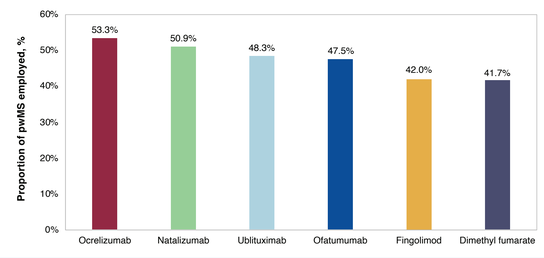
Key Model Assumptions

- Key assumptions consistent with published CEAs in MS were as follows[4,5,7]:
  - PwMS transitioned between EDSS health states based on transition probabilities derived separately for people with relapsing MS (RMS) or secondary progressive MS (SPMS)
  - PwMS could transition only from RMS to SPMS and experienced a one-unit increase in EDSS score
  - PwMS experienced an increasing probability of death in each EDSS health state
- Assumptions specific to this analysis were as follows:
  - Baseline characteristics of the included population were based on the prevalent ocrelizumab-treated pwMS in the OPERA I/II trials[6] (NCT01247324/NCT01412333; **Supplemental Table S2**)
  - The model leveraged estimates of HRs for 6-month CDP from a published NMA[5]
  - PwMS were assumed to continue treatment for the duration of follow-up; however, treatment switching was captured in the model

RESULTS

- The estimated rate of employment among pwMS treated with ocrelizumab ranged from 58.6% (vs 56.7% to 58.3% with other DMTs) in Year 1 to 53.3% (vs 41.7% to 50.9% with other DMTs) in Year 10 (**Figure 3**)
- After 10 years, pwMS treated with ocrelizumab had 4.7% to 27.6% higher rates of employment vs those treated with other DMTs

Figure 3. Percentage of PwMS Who Were Employed After 10 Years by Treatment



pwMS, people with multiple sclerosis.

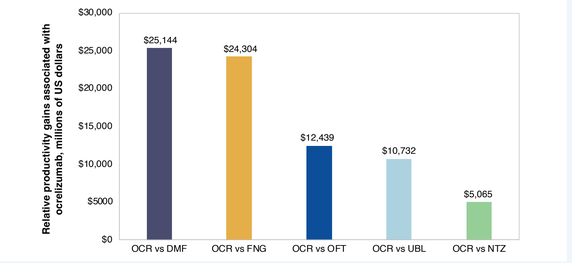
- When results were scaled to all prevalent MS cases in the US, total productivity losses over 10 years were lowest for pwMS treated with ocrelizumab ($96,037 million) compared with other DMTs in the US (**Table 5**)

Table 5. Population-Level Productivity Losses Over 10 Years by Treatment

Millions of US dollars	Lost market productivity	Lost nonmarket productivity	Total productivity loss
Ocrelizumab	$75,110	$20,927	$96,037
Natalizumab	$79,169	$21,933	$101,102
Ublituximab	$83,708	$23,060	$106,769
Ofatumumab	$85,075	$23,401	$108,476
Fingolimod	$94,566	$25,775	$120,341
Dimethyl fumarate	$95,231	$25,951	$121,181

- Ocrelizumab treatment was associated with relative productivity gains between $5065 million and $25,144 million US dollars vs other DMTs (**Figure 4**)

Figure 4. Productivity Gains Associated With Ocrelizumab vs Comparators After 10 Years



DMF, dimethyl fumarate; FNG, fingolimod; NTZ, natalizumab; OCR, ocrelizumab; OFT, ofatumumab; UBL, ublituximab.

LIMITATIONS

Table 6. Strengths and Limitations

Strengths	
Model structure and design	• This study relies on a published NMA[5] for 6-month CDP inputs and does not rely on an NMA conducted by Roche/Genentech • The structure of the model is consistent with a published CEA[4,5] and does not rely on modeling decisions made by Roche/Genentech
Limitations	
Heterogeneity in clinical trials	• Clinical trials vary in their study populations and definitions of CDP, which limited the NMA • Confirmed disability improvement was not measured in all DMT trials and was therefore excluded from the NMA and the model
Generalizability	• Model does not account for uncertainty in the HRs for 6-month CDP and does not evaluate statistically significant differences in outcomes • Results are based on CDP observed in clinical trials and may not be generalizable to real-world populations with MS • This study did not include all DMTs approved for the treatment of MS since data was not available for all DMTs in the NMA and the study focused on the most frequently used DMTs in the US
Productivity outcomes	• MS-specific nonmarket productivity estimates are lacking in the literature; therefore, a published algorithm[9] was used to estimate nonmarket productivity • The model uses a published crosswalk between PDDS and EDSS[8] to estimate productivity outcomes by EDSS; however, there is no validated crosswalk between PDDS and EDSS

CDP, confirmed disability progression; CEA, cost-effectiveness analysis; DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; HR, hazard ratio; MS, multiple sclerosis; NMA, network meta-analysis; PDDS, Patient-Determined Disease Steps.

CONCLUSIONS

- A higher percentage of pwMS treated with ocrelizumab were predicted to remain employed vs pwMS treated with other DMTs
- Over 10 years, productivity losses were lowest with ocrelizumab compared with other DMTs, highlighting the potential long-term benefits of treatment with ocrelizumab for pwMS, employers and society
- The use of DMTs that can delay disability progression, such as ocrelizumab, is predicted to increase employment and work productivity and provide benefits to patients, employers and society; however, further research is needed to examine the impact of specific DMTs on employment outcomes in the real world

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DISCLOSURES

C.K. Geiger, K.L. Rosettie, F. El Moustaid and **N.G. Bonine** are employees of Genentech, Inc., and shareholders of F. Hoffmann-La Roche Ltd.
R.B. McQueen receives consulting fees from Stage Analytics, which receives funding from Genentech, Inc. However, R.B. McQueen received no funding directly or through Stage Analytics to contribute to this research.

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