Cost-effectiveness of Glatiramer Acetate and Natalizumab in Relapsing-Remitting Multiple Sclerosis in the Presence of Long-Term Clinical Evidence

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ABSTRACT

OBJECTIVE: To assess lifetime cost-effectiveness of glatiramer acetate (GA) compared to natalizumab (NZ) in patients diagnosed with relapsing-remitting multiple sclerosis (RRMS) in the presence of long-term clinical evidence.

METHODS: A literature-based Markov model was developed with patients transitioning through health states based on the Kurtzke Expanded Disability Status Scale (EDSS). Patients in the model were at least 21 years of age, had been diagnosed with RRMS, and started in any of the health states at diagnosis. Patients with an EDSS score below 6.0 received treatment. Treatment effects for relapse and disease progression were obtained from clinical trials and long-term clinical evidence where available. Transition rates were estimated by applying a percent reduction of treatment effects of therapies to natural history rates of relapse and disease progression. Rates were adjusted for treatment discontinuation and persistent NZ antibodies. Patients incurred drug, other medical, and lost worker productivity costs. Patients on NZ incurred additional costs for monitoring, diagnosis, and treatment of progressive multifocal leukoencephalopathy, a possible serious adverse event for patients on NZ. Utility weights for each health state were taken from published utility assessments for people with RRMS. The primary outcomes of the model were lifetime costs and quality-adjusted life years (QALYs). Costs (2005US$) and outcomes were discounted at 3% annually.

RESULTS: The lifetime costs per patient for GA were $430,242 and for NZ were $498,728. QALYs during the lifetime of a patient on GA were 9.303 and 9.300 for a patient on NZ. The incremental costs per QALY for patients on GA and NZ compared to symptomatic treatment alone were $208,879 and $525,463, respectively. GA is cost-saving when compared to NZ. Progressive multifocal leukoencephalopathy had very little impact on results.

CONCLUSIONS: While incorporating all the long-term clinical evidence, model results indicated that GA was both less costly and more effective over a patient's lifetime than NZ in treating RRMS.

BACKGROUND

- Multiple sclerosis (MS) is a chronic, neurodegenerative inflammatory disease of the central nervous system that has been diagnosed in approximately 400,000 people in the United States.[1-3]
- Three main types of MS are generally recognized:[4,5]
  - Relapsing-remitting MS (RRMS) (most prevalent),
  - Secondary progressive MS (SPMS),
  - Primary progressive/relapsing MS (PPMS or PRMS),
- Prior to the introduction of the immunomodulating therapies for MS, treatment options consisted of symptomatic treatment such as physical therapy and drug therapy to manage symptoms.[1]
- Symptomatic treatment has been supplemented by new classes of immunomodulatory therapies approved for the treatment of RRMS:
  - Major histocompatibility complex (MHC) class II modulator (glatiramer acetate [GA]),
  - Selective adhesion-molecule (SAM) inhibitor (natalizumab [NZ]),
  - Interferon beta.

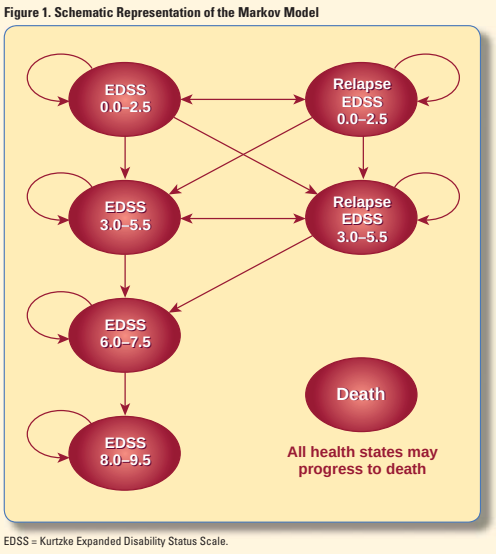
OBJECTIVE

To assess lifetime cost-effectiveness of GA compared to NZ in patients diagnosed with RRMS in the presence of long-term clinical evidence.

METHODS

A literature-based Markov model was developed with RRMS patients transitioning through health states based on the Kurtzke Expanded Disability Status Scale (EDSS) (Figure 1).

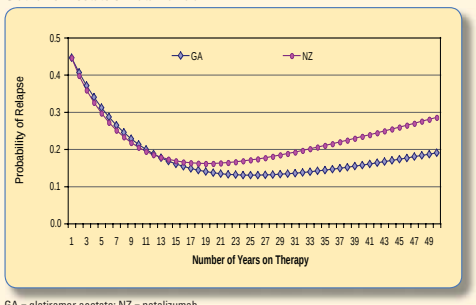
Figure 1. Schematic Representation of the Markov Model



EDSS = Kurtzke Expanded Disability Status Scale.

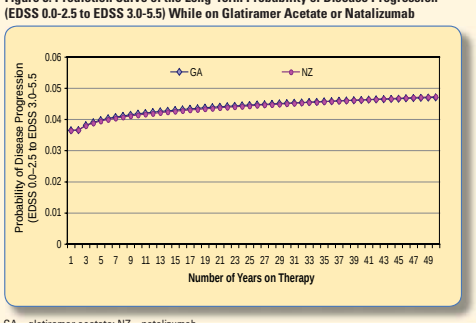
- The model was developed with a lifetime time horizon with 1-month transitions between health states.
- Per product labels, only patients needing a reduction in the frequency of clinical exacerbations were eligible for therapy.
- Relapse and disease progression rates for symptomatic treatment were obtained from natural history studies as reported in a previous model (Table 1).[6]
- GA and NZ treatment effects for relapse and disease progression were obtained from clinical trials.[7-8] Transition rates were estimated by applying a percent reduction of treatment effects of GA and NZ to natural history rates. Rates were mapped and fitted to prediction curves over time to estimate the long-term treatment effects (Figures 2-4).

Figure 2. Prediction Curve of the Long-Term Probability of Relapse While on Glatiramer Acetate or Natalizumab



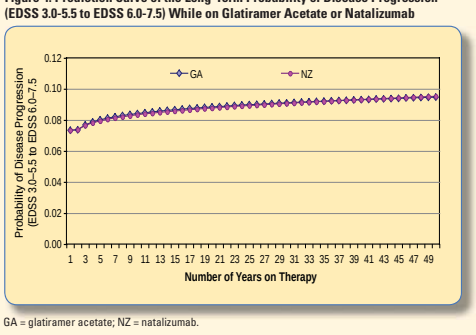
GA = glatiramer acetate; NZ = natalizumab.

Figure 3. Prediction Curve of the Long-Term Probability of Disease Progression (EDSS 0.0-2.5 to EDSS 3.0-5.5) While on Glatiramer Acetate or Natalizumab



GA = glatiramer acetate; NZ = natalizumab.

Figure 4. Prediction Curve of the Long-Term Probability of Disease Progression (EDSS 3.0-5.5 to EDSS 6.0-7.5) While on Glatiramer Acetate or Natalizumab



GA = glatiramer acetate; NZ = natalizumab.

- Rates of discontinuation were obtained from the clinical trails for GA and NZ. A relative 3% annual discontinuation was assumed when data were not available.[9]
- To account for persistent NZ antibodies, which increase a person's chance of relapse, the probabilities of relapse for patients on NZ were adjusted to reflect a weighted average of those with persistent NZ antibodies and those without (incidence of persistent NZ antibodies = 6.0%).[8]
- Mortality for a patient was based on age-specific all-cause mortality and progression through all the health states (e.g., EDSS 10 = death).[1,10]
- Patients incurred drug, other medical, and lost worker productivity costs and utilities for each health state (Table 1).
- Patients on NZ incurred additional costs for administration of NZ and for monitoring, diagnosis, and treatment of progressive multifocal leukoencephalopathy, a possible serious adverse event for patients on NZ (Table 1).
- Costs (2005US$) and outcomes were discounted at 3% annually.

Table 1. Summary of Parameters and Values Used in Base Case Model

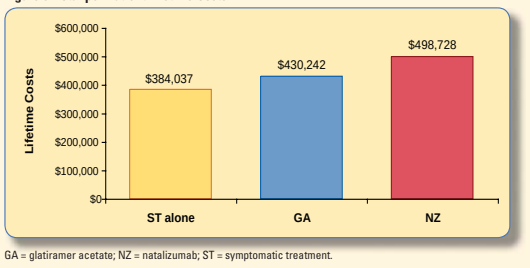
Parameter Description	EDSS 0.0-2.5	EDSS 3.0-5.5	Relapse EDSS 0.0-2.5	Relapse EDSS 3.0-5.5	EDSS 6.0-7.5	EDSS 8.0-9.5
Initial patient distribution[11]	26.4%	58.7%	0.0%	0.0%	13.8%	1.1%
Monthly probability of disease progression for ST alone (to next EDSS health state)	0.0044	0.0092	0.0044	0.0092	0.0036	0.0010
Monthly probability of relapse for ST alone	0.0755	0.0755	NA	NA	NA	NA
Health-state-specific MS-related monthly costs[11]	$377.08	$785.07	$371.81	$1,041.04	$1,938.84	$3,447.96
Lost worker productivity cost[12-14]	GA = $875.15 NZ = $820.53				Patients not employed	
Utility weights[8,15]	0.824	0.679	0.730	0.585	0.533	0.491
Monthly drug acquisition costs (WAC)[16]	GA = $1,258.20 NZ = $1,996.16				GA or NZ not administered	
Additional monthly NZ costs	Administration cost per administration = $161.82[17,18] Monthly costs for monitoring, diagnosis, and treatment of PML = $20.50[18,19]				NZ not administered	

EDSS = expanded disability status scale; GA = glatiramer acetate; MS = multiple sclerosis; NA = not applicable; NZ = natalizumab; PML = progressive multifocal leukoencephalopathy; ST = symptomatic treatment; WAC = wholesale acquisition cost.

RESULTS

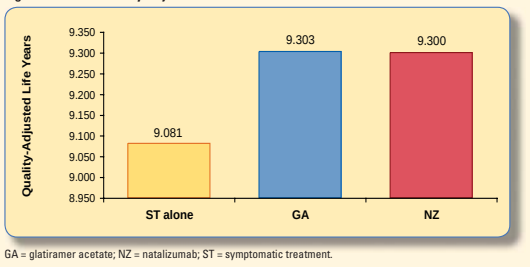
- Base case model results indicated that GA and NZ were both more effective and more costly than symptomatic treatment alone in treating RRMS over a patient's lifetime.
- The incremental costs per quality-adjusted life year (QALY) (vs. symptomatic treatment alone) were $208,879 for GA and $525,463 for NZ.
- Base case model results also indicated that GA was less costly and more effective than NZ in treating RRMS over a patient's lifetime.
- Setting the monthly incidence of progressive multifocal leukoencephalopathy to 0% (base case 0.004%) results in a lifetime cost per patient of $499,064 and 9.307 QALYs for patients on NZ.

Figure 5. Total per Patient Lifetime Costs



GA = glatiramer acetate; NZ = natalizumab; ST = symptomatic treatment.

Figure 6. Lifetime Quality-Adjusted Life Years



GA = glatiramer acetate; NZ = natalizumab; ST = symptomatic treatment.

CONCLUSIONS

- Both GA and NZ were more effective and more costly than symptomatic treatment alone in treating RRMS, and GA was the most cost-effective versus symptomatic treatment alone.
- While incorporating all the long-term clinical evidence, model results indicated that GA was both less costly and more effective over a patient's lifetime than NZ in treating RRMS.

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