Feasibility Assessment of Using MiToS Staging System for Conducting Health Economic Analysis in Amyotrophic Lateral Sclerosis (ALS)

Paulos Gebrehiwet,¹ Saurabh Aggarwal,² Ozlem Topaloglu,² Adriano Chiò³

¹Cytokinetics, Incorporated, South San Francisco, CA, USA; ²Novel Health Strategies, Bethesda, MD, USA; ³Rita Levi Montalcini Department of Neuroscience, University of Turin, Turin, Italy

INTRODUCTION & OBJECTIVE

- Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease that carries a considerable economic burden for patients, families, and healthcare systems, as well as high indirect costs due to productivity losses.¹
- Progression of ALS can be measured using the Milano-Torino staging (MiToS) system.
- Progression between stages is based on functional ability, defined by loss of autonomy involving the 4 key domains: walking/self-care, swallowing, communicating, and breathing.²
- The value of MiToS for cost-effectiveness modeling has not been

RESULTS

- For each hypothetical treatment effect, maximum gains of QALYs and LYs were realized at the 10-year horizon in all 3 scenarios of patient distribution.
- Results for Scenario 3 (patient distribution from the PRO-ACT database) are shown in **Table 4**; results for Scenarios 1 and 2 showed a similar pattern (**Supplementary Tables S1** and **S2***).
- The lifetime (20-year horizon) analysis did not improve either QALYs or LYs in any material way compared with the 10-year horizon.
- For a 10-year time horizon, incremental QALYs and LYs for the

Table 4. QALY and LY for hypothetical treatment effect forProduct X vs SoC

Patient distribution based on Thakore et al⁴ (Scenario 3)

| | QALY | | Incremental QALY | LY | | Incremental LY | |
|----------|-----------|------|---------------------|-----------|------|---------------------|--|
| RR | Product X | SoC | Product X vs SoC | Product X | SoC | Product X vs SoC | |
| 1-year h | orizon | | | | | | |
| 0.80 | 0.59 | 0.58 | 0.01 | 0.97 | 0.96 | 0.01 | |
| 0.75 | 0.60 | 0.58 | 0.02 | 0.97 | 0.96 | 0.01 | |
| 0.70 | 0.60 | 0.58 | 0.02 | 0.97 | 0.96 | 0.01 | |
| 0.65 | 0.61 | 0.58 | 0.03 | 0.97 | 0.96 | 0.01 | |
| 5-year h | orizon | | | | | | |
| 0.80 | 1.39 | 1.16 | 0.22 | 2.76 | 2.33 | 0.42 | |
| 0.75 | 1.45 | 1.16 | 0.29 | 2.88 | 2.33 | 0.54 | |
| 0.70 | 1.52 | 1.16 | 0.36 | 3.00 | 2.33 | 0.67 | |
| 0.65 | 1.60 | 1.16 | 0.44 | 3.14 | 2.33 | 0.80 | |
| 10-year | horizon | | | | | | |
| 0.80 | 1.43 | 1.18 | 0.26 | 2.90 | 2.37 | 0.53 | |
| 0.75 | 1.52 | 1.18 | 0.34 | 3.07 | 2.37 | 0.70 | |
| 0.70 | 1.61 | 1.18 | 0.44 | 3.26 | 2.37 | 0.89 | |
| 0.65 | 1.72 | 1.18 | 0.55 | 3.48 | 2.37 | 1.11 | |
| 20-year | horizon | | | | | | |
| 0.80 | 1.43 | 1.18 | 0.26 | 2.90 | 2.37 | 0.53 | |
| 0.75 | 1.52 | 1.18 | 0.34 | 3.08 | 2.37 | 0.70 | |
| 0.70 | 1.62 | 1.18 | 0.44 | 3.27 | 2.37 | 0.90 | |
| 0.65 | 1.73 | 1.18 | 0.55 | 3.50 | 2.37 | 1.12 | |

established, and the objective of this study was to assess feasibility of using MiToS for developing a Markov model to conduct economic analysis in ALS.

METHODS

Overview

- A hypothetical treatment ("Product X") was compared with standard of care for ALS.
- The model framework was based on MiToS staging and included 6 states: stage 0 indicates no functional domains lost, stages 1–4 indicate loss of 1 to 4 functional domains, respectively, and stage 5 is death (Figure 1).
- Time horizons of 1, 5, and 10 years and lifetime (20-year horizon) were examined, with 3-month cycle length and half-cycle correction.
- Although people with ALS survive an average of 2–3 years from diagnosis, a small proportion live for ≥10 years; hence a 20-year horizon ensured the cost-effectiveness model would continue until all patients reached the death state (lifetime analysis).



hypothetical treatment effects are shown in Figure 2.

- With a hypothetical patient distribution with all patients starting in stage 0, the range of incremental QALYs and LYs was 0.28–0.60 and 0.56–1.17, respectively.
- With patient distributions based on real-world evidence settings, the range of incremental QALYs and LYs was 0.21–0.55 and 0.46–1.11, respectively.
- Analysis of QALYs by MiToS stages showed the majority of gains occur in earlier stages, especially stages 0, 1, and 2 (Table 5; Supplementary Table S3*).
- One-way sensitivity analysis for QALYs showed that model results were most sensitive to treatment effect and discount rate for efficacy. Most other variables had similar effects on overall model results.
- There are some evidence gaps for US costs and health utilities.

Figure 2. Incremental QALYs and LYs for hypothetical treatment effect for Product X vs SoC for 10-year horizon

A. Patient distribution: Scenario 1 (Hypothetical)



LY, life-year; QALY, quality-adjusted life-year; RR, relative risk; SoC, standard of care

Table 5. QALY for Product X with RR of 0.65 vs SoC for each MiToS stage

Patient distribution based on Thakore et al⁴ (Scenario 3)

| | QALY | | Incremental QALY | | | |
|-----------------|-----------|------|------------------|--|--|--|
| | Product X | SoC | Product X vs SoC | | | |
| 1-year horizon | | | | | | |
| Stage 0 | 0.46 | 0.41 | 0.05 | | | |
| Stage 1 | 0.12 | 0.13 | -0.01 | | | |
| Stage 2 | 0.02 | 0.03 | -0.01 | | | |
| Stage 3 | 0.00 | 0.01 | 0.00 | | | |
| Stage 4 | 0.00 | 0.00 | 0.00 | | | |
| Total | 0.61 | 0.58 | 0.03 | | | |
| 5-year horizon | | | | | | |
| Stage 0 | 0.80 | 0.56 | 0.24 | | | |
| Stage 1 | 0.46 | 0.33 | 0.13 | | | |
| Stage 2 | 0.19 | 0.15 | 0.05 | | | |
| Stage 3 | 0.08 | 0.06 | 0.02 | | | |
| Stage 4 | 0.07 | 0.07 | 0.00 | | | |
| Total | 1.60 | 1.16 | 0.44 | | | |
| 10-year horizon | | | | | | |
| Stage 0 | 0.81 | 0.56 | 0.25 | | | |
| Stage 1 | 0.49 | 0.33 | 0.16 | | | |
| Stage 2 | 0.22 | 0.15 | 0.07 | | | |
| Stage 3 | 0.10 | 0.07 | 0.03 | | | |
| Stage 4 | 0.10 | 0.07 | 0.03 | | | |
| Total | 1.72 | 1.18 | 0.55 | | | |
| 20-year horizon | | | | | | |
| Stage 0 | 0.81 | 0.56 | 0.25 | | | |
| Stage 1 | 0.49 | 0.33 | 0.16 | | | |
| Stage 2 | 0.22 | 0.15 | 0.07 | | | |
| Stage 3 | 0.10 | 0.07 | 0.03 | | | |
| Stage 4 | 0.10 | 0.07 | 0.03 | | | |
| Total | 1.73 | 1.18 | 0.55 | | | |
| | | | | | | |

Figure 1. MiToS-based model structure

MiToS, Milano-Torino staging

Health Utilities

 EQ-5D-5L scores for MiToS-based health states (Table 1) were previously reported by Moore et al.³

Table 1. EQ-5D-5L scores for MiToS stages

| | EQ-5D-5L utility, mean (95% CI) |
|-------------------------------|---|
| Stage 0 | 0.71 (0.69–0.73) |
| Stage 1 | 0.48 (0.44–0.51) |
| Stage 2 | 0.36 (0.31–0.42) |
| Stage 3 | 0.33 (0.23–0.43) |
| Stage 4 | 0.25 (0.07–0.42) |
| CL confidence interval: EO-50 | 0-51 EuroOol 5-dimension 5-level: MiToS Milano-Torino staging |

Transition Probabilities

 The 3-month transition probabilities for standard of care (Table 2) were obtained from Thakore et al.⁴

Table 2. Transition probability matrix for standard of care

| | Stage 0 | Stage 1 | Stage 2 | Stage 3 | Stage 4 | Dead |
|---------|---------|---------|---------|---------|---------|-------|
| Stage 0 | 0.714 | 0.232 | 0.04 | 0.006 | 0.001 | 0.007 |
| Stage 1 | 0.094 | 0.605 | 0.199 | 0.042 | 0.010 | 0.050 |
| Stage 2 | 0.013 | 0.164 | 0.435 | 0.177 | 0.066 | 0.145 |
| Stage 3 | 0.001 | 0.025 | 0.126 | 0.330 | 0.269 | 0.249 |
| Stage 4 | 0 | 0.002 | 0.018 | 0.101 | 0.574 | 0.305 |
| Dead | 0 | 0 | 0 | 0 | 0 | 1 |

B. Patient distribution: Scenario 2 (RWE, Moore et al³)



C. Patient distribution: Scenario 3 (RWE, Thakore et al⁴)

MiToS, Milano-Torino staging; QALY, quality-adjusted life-year; RR, relative risk; SoC, standard of care

CONCLUSIONS

- MiToS-based staging can be used for developing a Markov model for economic analysis in ALS.
- A hypothetical new treatment with 20–35% RRR using MiToS can lead to significant QALYs and LYs gains in ALS.
- Irrespective of the treatment effect, a 10-year time horizon is appropriate for MiToS-based cost-effectiveness analysis in ALS; this is consistent with the disease as only few patients survive for >10 years from onset.

Treatment Effect

- Treatment effect for the hypothetical intervention (Product X), was assumed to be reduced risk of progressing to the next MiToS stage.
- Four options were evaluated, with relative risk reduction (RRR) vs
- standard of care of 20%, 25%, 30%, or 35%.

Patient Distribution

• We tested 3 scenarios: in Scenario 1, all patients started in Stage 0, in Scenarios 2 and 3, the distribution was based on real-world evidence (**Table 3**).

Table 3. Patient distribution scenarios

| | Patie | | | | | |
|------------------------------|-------|-------|-------|------|------|----------------------------|
| | 0 | 1 | 2 | 3 | 4 | Source |
| Scenario | | | | | | |
| 1 | 100 | 0 | 0 | 0 | 0 | Assumption |
| 2 | 50.59 | 33.28 | 12.69 | 3.03 | 0.84 | Moore et al ³ |
| 3 | 80.3 | 18.3 | 1.3 | 0.1 | 0 | Thakore et al ⁴ |
| MiToS, Milano-Torino staging | | | | | | |

Model Outcomes

Quality-adjusted life years (QALYs) and life-years (LYs) with a 3% discount rate were reported.



LY, life-year; QALY, quality-adjusted life-year; RWE, real-world evidence; SoC, standard of care

References

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Disclosures

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