AMX0035 and Oral Edaravone for Amyotrophic Lateral Sclerosis

Public Meeting — August 19, 2022

Meeting materials available at: https://icer.org/assessment/amyotrophic-lateral-sclerosis-2022/#timeline

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Clinical and Patient Experts

Aaron Lewis, MD, Neurologist, Neuromuscular Medical Director, ALS Multidisciplinary Clinic, Kaiser Permanente

- *Dr. Lewis received $10,000 grant from the ALS Association in support of ALS patients treated at their clinic.*

Richard Bedlack, MD, PhD, Professor of Neurology, Director of ALS Clinic, Duke University School of Medicine

- *Dr. Bedlack has received consulting support in excess of $5,000 and research support from the ALS Association and Amylyx.*

Joel Shamaskin, MD, Person with ALS and Retired Professor Emeritus of Medicine, University of Rochester School of Medicine and Dentistry

- *Dr. Shamaskin serves on the ALS Association research committee.*

Cathy Collet, BS, MS, ALS Patient Advocate

- *Ms. Collet is a past employee of Eli Lilly and received a vested pension benefit. She also owns more than $10,000 in Eli Lilly shares.*

Why Are We Here Today?

“The initial symptoms are frustrating and worrisome, regardless of how fast or slow they come on. You need to find support, how to prepare your house and life for this. You need moral and psychological support. You have family who are often just as upset if not more upset than you are. A major preoccupation is trying to figure out the extended period of time where you need expensive homecare. It makes you wonder if you’re going to bankrupt your family.”

Person with ALS

Why Are We Here Today?

- What happens the day these treatments receive FDA approval?
- Questions about:
  - Evidence – what are the risks and benefits?
  - How do new treatments fit into the evolving landscape?
  - What are reasonable prices and costs to patients, the health system, and the government?
  - What lessons are being learned to guide our actions in the future?

The Impact on Rising Health Care Costs for Everyone

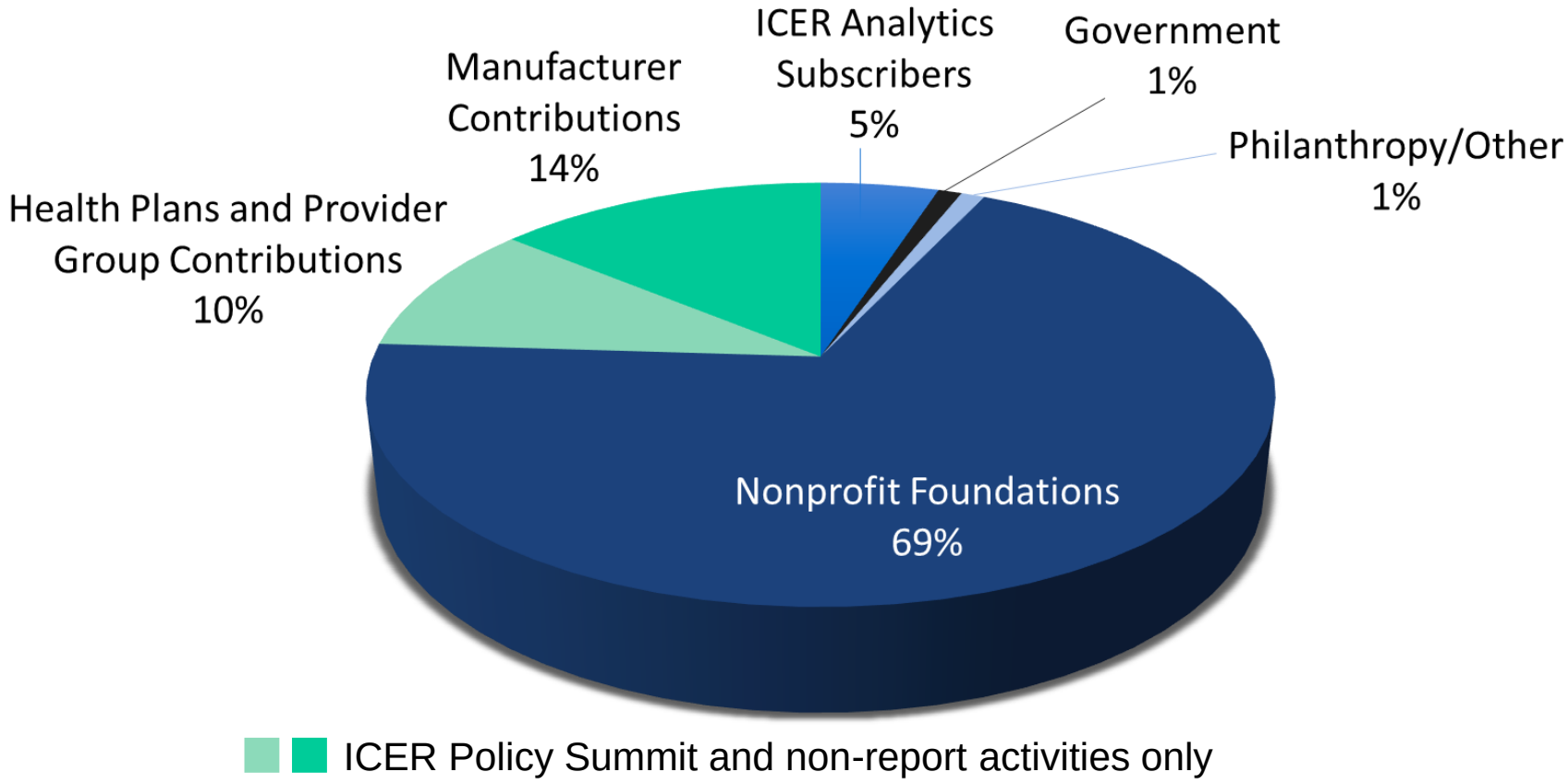
https://khn.org/news/article/diagnosis-debt-investigation-100-million-americans-hidden-medical-debt/

Organizational Overview

- Midwest Comparative Effectiveness Public Advisory Council (CEPAC)
- The Institute for Clinical and Economic Review (ICER)

Sources of Funding, 2022

https://icer.org/who-we-are/independent-funding/



How Was the ICER Report Developed?

- Scoping with guidance from patients, clinical experts, manufacturers, and other stakeholders
- Internal ICER staff evidence analysis and cost-effectiveness modeling
- Public comment and revision
- Expert reviewers
  - **Richard S. Bedlack Jr., MD, PhD, MS,** Professor of Neurology and Director, ALS Clinic, Duke University School of Medicine
  - **Ken Menkhaus, PhD,** Person with ALS and Professor of Political Science, Davidson College
  - **Joel Shamaskin, MD,** Person with ALS and Retired Professor Emeritus of Medicine, University of Rochester School of Medicine and Dentistry
  - **John Turnbull, MD, PhD,** Andrew Bruce Douglas Chair in Neurology, McMaster University
- How is the evidence report structured to support CEPAC voting and policy discussion?

Value Assessment Framework: Long-Term Value for Money

Agenda

Time (CDT)	Activity
9:30am—9:50am	**Meeting Convened and Opening Remarks** Steven D. Pearson, MD, MSc President, Institute for Clinical and Economic Review
9:50am—10:35am	**Presentation of the Clinical Evidence** Anil N. Makam, MD, MAS Assistant Professor of Medicine, UCSF
10:35am—11:20am	**Presentation of the Economic Model** Kangho Suh, PharmD, PhD Assistant Professor, School of Pharmacy, University of Pittsburgh
11:20am – 12:00pm	**Lunch Break**
12:00pm – 12:10pm	**Manufacturer Public Comments and Discussion**
12:10pm—12:40pm	**Public Comments and Discussion**
12:40pm—1:50pm	**Midwest CEPAC Vote on Clinical Effectiveness and Value**
1:50pm—2:00pm	**Break**
2:00pm—3:30pm	**Policy Roundtable**
3:30pm—4:00pm	**Reflections from Midwest CEPAC**
4:00pm	**Meeting Adjourned**

Presentation of the Clinical Evidence

Anil N. Makam, MD, MAS

Evidence Author, ICER

Assistant Professor of Medicine, UCSF

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Key Collaborators

- Rasheed Mohammed, PharmD, MPH, Fellow, ICER
- Avery McKenna, BS, Senior Research Assistant, ICER
- Dmitriy Nikitin, MSPH, Research Lead, ICER

Disclosures:

Anil Makam received funding from ICER for this report

Background: Amyotrophic Lateral Sclerosis

- ALS is a rare, rapidly progressive & fatal disease that causes loss of motor neurons in the brain & spinal cord
- Presentation is variable
  - 2/3rd limb onset; 1/3rd bulbar onset
  - Progresses from weakness to paralysis, respiratory failure, & death
- Average life expectancy is 3-5 years after symptom onset
  - 1 in 10 are ‘slow progressors’ and survive >10 years

Background: Epidemiology

- **Incidence**: 2 per 100,000 persons are newly diagnosed
- **Prevalence**: ~25,000 people in the US
- **Etiology:** mostly unknown; mix of genetics, environment, & aging
  - 90% Sporadic; 10% Familial
  - Risks: Age (60-79 year olds), Male sex, White race, & military service
- **Cost:** $1 billion annually to society

Background: Standard of Care & Management

- **Diagnosis**: clinical; often delayed ~1 year after symptom onset
- **Prognosis:** worse if older, bulbar onset, fast progression, ↓ lung function
- **Treatment:** no cure
  - Symptom management, nutrition, & noninvasive ventilation via ALS centers
  - Riluzole & edaravone are the only 2 FDA-approved drugs to slow progression
    - Riluzole (oral) prolongs survival by ~2 months & recommended by guidelines
    - IV edaravone not endorsed by AAN and is not approved for use in Europe

Insights from Discussions with Patients & Caregivers

- Diverse range of experiences in symptoms & progression
- Caregiver needs & burden are profound: time, stress, health, financial
- Enthusiasm for new treatments with high tolerance of risk
- Treatment burden & costs are major barriers to try new treatment
  - Only some use IV edaravone: limited evidence, catheter risks, infusion burden, cost
  - Enthusiasm for oral drugs: most use riluzole & expressed interest in oral edaravone

Two New Medications

AMX0035

- Oral combination of two drugs (PB & TURSO)
- Theoretical MOA: target two different mechanisms of neuronal death
- Daily for 3 weeks, and then up to twice a day after
- FDA AdCom voted 6-4 against March 30th, reconvening Sept 7th; decision Sept 29th

Oral Edaravone (Radicava ORS®)

- Has identical dosing as the IV formulation:
- Theoretical MOA: free radical scavenger
- FDA approved on May 12, 2022 based on bioequivalence

Scope of Review

- **Scope:** Clinical & cost effectiveness of adding AMX0035 or oral edaravone to standard of care (SOC)

- **Population:** Adults with ALS

- **Interventions and Comparators:**
  - AMX0035 vs. SOC (riluzole ± IV edaravone ± multidisciplinary care)
  - Oral edaravone vs. SOC (riluzole ± multidisciplinary care)
  - No head-to-head comparison

Clinical Evidence

Primary Outcome for all ALS trials: ALSFRS-R

- 12 items each scored 0-4
- Higher is better; max of 48
- No established MCID
  - ALS MDs: ≥ 20% Δ meaningful
  - Stakeholders:1-point change is modest but still important

Domain	Item
Bulbar	Speech
	Salivation
	Swallowing
Fine Motor	Handwriting
	Cutting Food
	Dressing and Hygiene
Gross Motor	Turning in bed
	Walking
	Climbing Stairs
Respiratory	Dyspnea
	Orthopnea
	Respiratory Insufficiency

AMX0035: Overview of Evidence

- CENTAUR: 24-week phase 2 trial of early-stage ALS (n=137)
  - Inclusion: definite ALS, symptom onset ≤ 18 months, SVC >60%
  - 2:1 randomization from 25 centers in Northeast ALS consortium

- CENTAUR-OLE: extension up to 30 months (n=137 for survival)
  - 66% enrolled into OLE (n=90)
  - Survival assessed in ITT using vital status sweep of public records

AMX0035 on Function (ALSFRS-R)

- 2.3 points (95% CI: 0.2-4.5) ≈ 25% slowing of functional decline
  - Excluded 2 early deaths in treatment arm
  - Joint rank (combines function & survival): p-value=0.037

- FDA re-analyses with lower efficacy & statistical persuasiveness
  - ALSFRS-R difference of 1.7 points, p=0.11 (modeled non-linearity)
  - Joint rank: p=0.079 (multiple imputation for missing data)

ALSFRS-R: ALS functional rating scale-revised

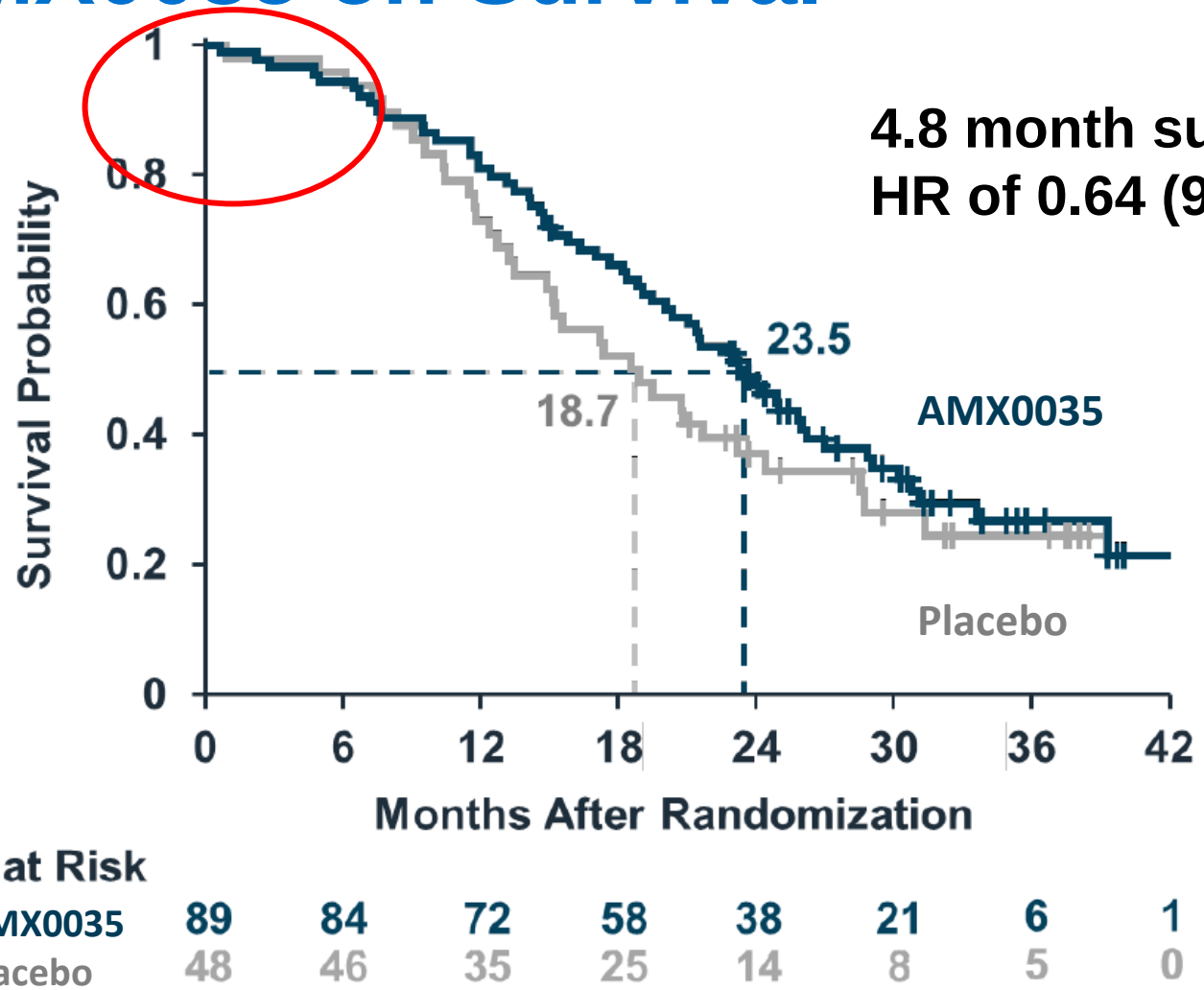
AMX0035 on Secondary Outcomes

- Secondary outcomes not significant, but favored AMX0035
  - Isometric muscle strength (ATLIS): +2.8 (-0.7 to 6.3), p=0.11
  - Slow vital capacity (SVC): +5.1% (-0.5 to 10.8), p=0.08

- Exploratory biomarker not significant, but favored placebo
  - Hard to measure in plasma & experts doubt its validity

p-NF-H: phosphorylated neurofilament heavy chain protein

AMX0035 on Survival



4.8 month survival gain
HR of 0.64 (95% CI: 0.42-0.99), p=0.048

Harms of AMX0035

- Minimal harms
- Diarrhea & nausea greatest in first 2 weeks (33% vs 20%)
- More discontinuation due to adverse effects (20% vs 10%)

ALSFRS-R: amyotrophic lateral sclerosis functional rating score-revised.

Uncertainty and Controversies for AMX0035

- Do findings **generalize** to more advanced ALS or minority populations?

- Are findings from the CENTAUR trial **valid**?
  - Randomization implementation error (sensitivity analyses reassuring)
  - Concern for unblinding: 73% of placebo correctly guessed assignment
  - FDA re-analyses found lower efficacy & statistical persuasiveness
  - Survival benefit not seen in RCT & out of proportion to functional gains
    - Ongoing phase 3 PHOENIX RCT (completed 2024)

- Is combination therapy of PB/TURSO **better** than TURSO alone?
  - Ongoing RCT of TURSO vs placebo (completed in 2023)

ICER Evidence Rating for AMX0035

Treatment	Population	Comparator	Evidence Rating
AMX0035	All ALS patients	Standard of care	C++

- **C++: Comparable or Better** – High certainty does not cause harm and moderate certainty of a comparable to substantial net health benefit

Oral Edaravone: Overview of Evidence

Three 24-week trials of IV edaravone in Japan (MCI-186)

- Study 16: negative phase 3 trial in early-stage ALS (n=205)
- Study 18: negative phase 3 trial in advanced ALS (n=25)
- *Post-hoc analysis of Study 16 found benefit in a subgroup (35% of cohort)*
- **Study 19: phase 3 in narrow & well-defined early-stage ALS (n=137)**

Edaravone on Function

	Change from Baseline in ALSFRS-R Score at Week 24		
Trial	**IV Edaravone**	**Placebo**	**Difference (95% CI), p-value**
Study 16	-5.70 ± 0.85	-6.35 ± 0.84	0.65 (-0.90 to 2.19), p=.41
Study 18	-6.52 ± 1.78	-6.00 ± 1.83	-0.52 (-5.62 to 4.58), p=.84
Study 19	**-5.01 ± 0.64**	**-7.50 ± 0.66**	**2.49 (0.99 to 3.98), p= 0.0013**

*33% slowing of functional decline

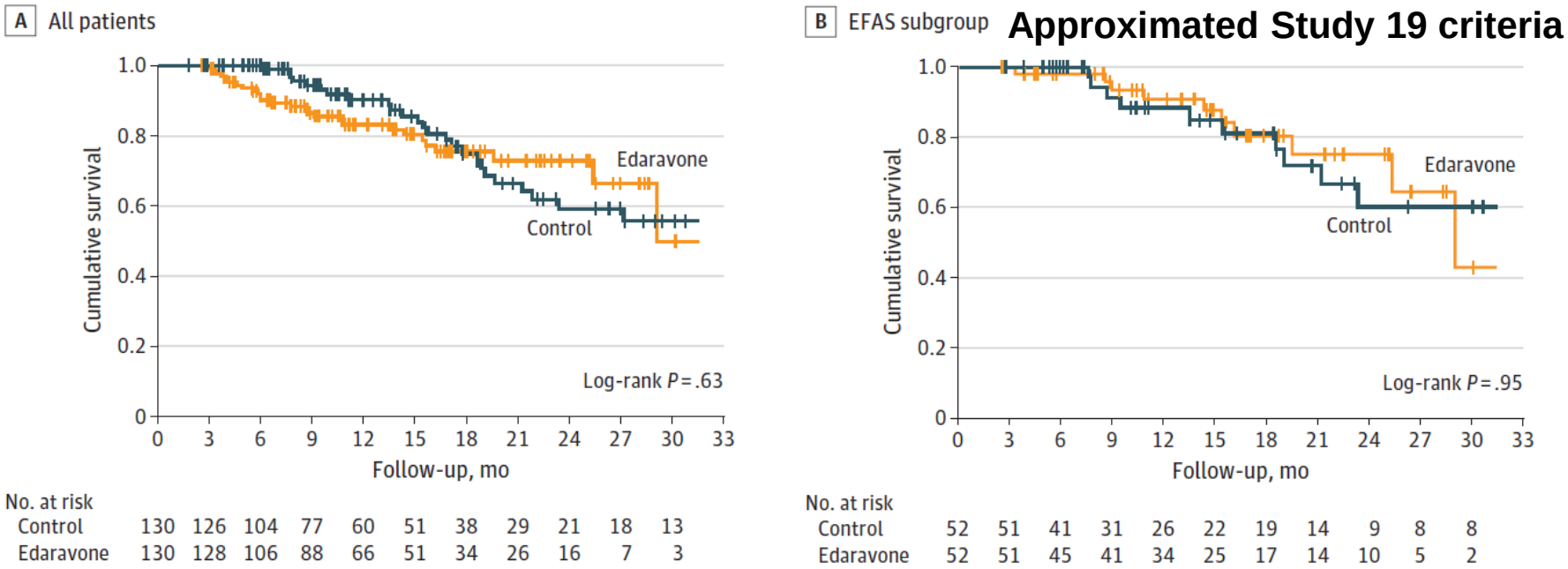
ALSFRS-R: ALS functional rating scale-revised

Edaravone on Secondary Outcomes

- **Quality of Life improved**: ALSAQ-40 of -8.8 (-16.8 to -0.8), p=.03
  - ALSAQ-40 ranges 40-100 with lower scores reflecting better QoL
- **Respiratory function** numerically favored edaravone
  - Forced vital capacity (FVC) difference of 4.8% (-0.8 to 10.4), p=0.09
- **Grip and pinch strength** were no different
- **Survival:** Only 3 deaths observed

No Survival Difference from Real-World Evidence

Figure 3. Kaplan-Meier Plots for Survival Probability During Follow-up



- 260 patients in 12 German ALS Centers; 104 approximated Study 19 criteria
- Controls matched on site of onset, age, duration, & baseline ALSFRS-R

Witzel et. al. *JAMA Neurology.* 2022

Harms of Edaravone

- Minimal harms in the trials compared to placebo infusion
- More contusions vs placebo (15% vs 9%)
- Oral formulation appears to be much safer than IV

ALSFRS-R: amyotrophic lateral sclerosis functional rating score-revised.

Uncertainty and Controversies for Oral Edaravone

- 2 of 3 trials of IV edaravone were negative
- Only studied in Japan, so uncertain generalizability
- Study 19 criteria only represents up to 10% of all ALS patients
- Assumed equivalent efficacy based on bioequivalence studies

ICER Evidence Ratings for Oral Edaravone

Treatment	Population	Comparator	Evidence Rating
Oral Edaravone	Meets narrow Study 19 criteria	Standard of care	C+
Oral Edaravone	Does not meet Study 19 criteria	Standard of care	I

- **C+: Comparable or Incremental** – high certainty it does not cause harm and a moderate certainty of a comparable or small net health benefit
- **I: Insufficient** – Not sure if it is effective and any harms could be net negative

Potential Other Benefits and Contextual Considerations

- Acuity of the need for treatment is extremely high
- Caregiver burden is considerable & likely underestimated
- Oral edaravone overcomes the burden & risk of IV formulation

Public Comments Received

- AMX0035: “include long-term tracheostomy/ventilation-free survival and hospitalization from the CENTAUR OLE”
- AMX0035: “include recently published data on crossover adjusted survival benefit”
- Edaravone: “evidence supporting clinical effectiveness…is robust”

Summary

- AMX0035 appears safe and may have a modest benefit on disease progression and a more substantial benefit for survival
  - Concerns about trial conduct, analytic choices, & inconsistencies
- Oral edaravone may slow progression modestly without a survival gain, but only for narrowly defined early-stage ALS
  - Concern about a small, single trial in a homogenous population
  - Oral edaravone is safe and overcomes burden & risks of IV therapy

Questions?

AMX0035 and Oral Edaravone for ALS: Effectiveness and Value

Kangho Suh, PharmD, PhD
Assistant Professor
School of Pharmacy
University of Pittsburgh

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Key Contributors

- Josh J. Carlson, PhD, MPH, Professor, CHOICE Institute, University of Washington
- Marina Richardson, MSc, Health Economist, ICER

Disclosures:

Kangho Suh and Josh Carlson received funding from ICER for this report

Objective

Estimate the lifetime cost-effectiveness of adding AMX0035 or oral edaravone to their respective standards of care compared to standard of care alone for the treatment of ALS.

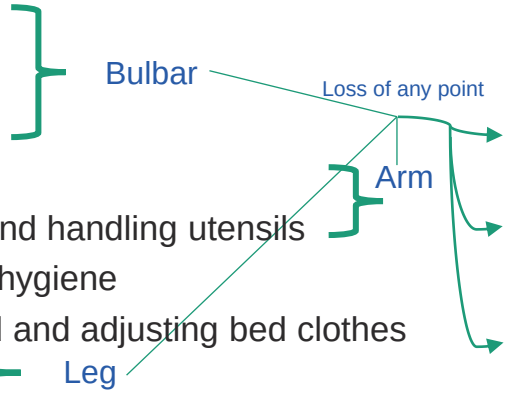
Methods in Brief

Methods Overview

- **Model**: Markov model
- **Setting**: United States
- **Perspective**: Health Care Sector Perspective
- **Time Horizon**: Lifetime
- **Discount Rate**: 3% per year (costs and outcomes)
- **Cycle Length**: 1 month
- **Primary Outcome**: Cost per quality-adjusted life year (QALY) gained; cost per life year (LY) gained; equal value of LYs gained (evLY)

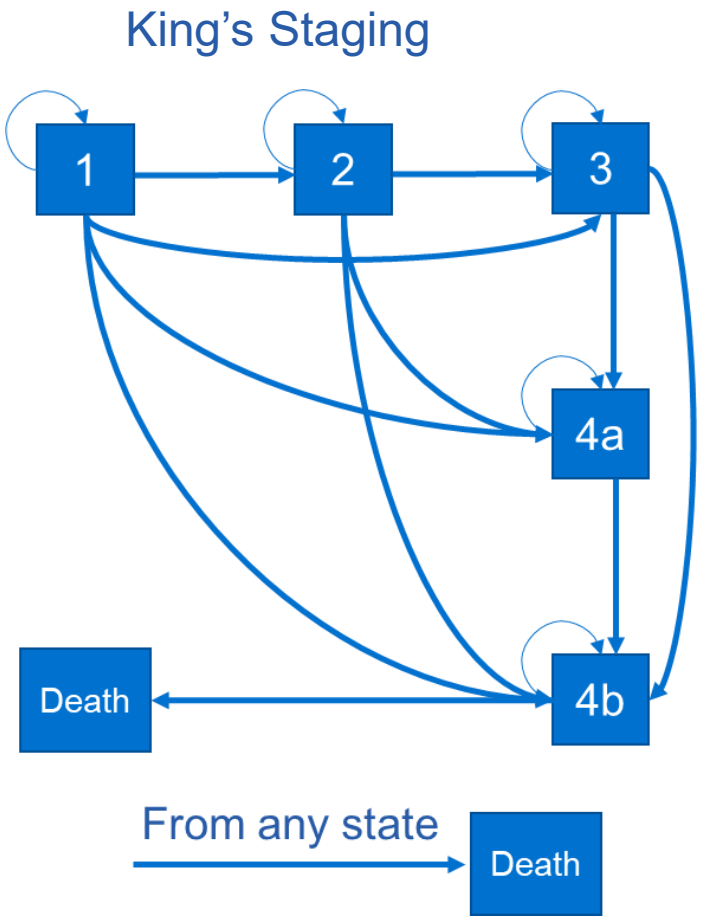
Determining King's Staging

- Markov staging in ALS based off of ALSFRS-R
- Measures 12 aspects of physical function
  - Each aspect scored from 0 – 4, with 0 representing no ability and 4 representing normal function
    - Speech
    - Salivation
    - Swallowing
    - Handwriting
    - Cutting food and handling utensils
    - Dressing and hygiene
    - Turning in bed and adjusting bed clothes
    - Walking
    - Climbing stairs
    - Dyspnea
    - Orthopnea
    - Respiratory insufficiency



State	King's
1	Functional involvement of one CNS region (bulbar, arm, or leg)
2	Functional involvement of two CNS regions
3	Functional involvement of three CNS regions
4a	Need for feeding tube
4b	Need for noninvasive ventilation (NIV)

Model Schematic



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1	Functional involvement of one CNS region (bulbar, arm, or leg)
2	Functional involvement of two CNS regions
3	Functional involvement of three CNS regions
4a	Need for feeding tube
4b	Need for noninvasive ventilation (NIV)

Model Characteristics

- Two separate ALS populations were modeled based on available data / evidence
  - AMX0035
  - Oral edaravone

Key Model Assumptions

- The relative treatment effect on progression of oral edaravone (hazard ratio [HR] of 0.665) is only applied to King's stage 1 through 3 and is constant across these stages.
- The proportion of patients who may receive treatment benefit of oral edaravone among all patients who receive treatment is 35%.
- Based on discontinuation data at six months from their respective pivotal trials, we applied a monthly discontinuation probability of 3.47% for AMX0035 and 0.23% for oral edaravone throughout the patient's lifetime

Key Model Inputs: Efficacy and Survival

Characteristic	Value	Source
AMX0035 RRR on disease progression	0.75	CENTAUR trial
AMX0035 HR on mortality	0.74	Calibrated from HR noted in FDA AdComm Meeting
Oral edaravone HR on disease progression	0.665	Study 19 and CADTH pharmacoeconomic report
Oral edaravone HR on mortality	1.0	Open label extension study

Key Model Inputs: Treatment Costs

Costs	Value	Source	Notes
AMX0035 annual cost	$169,000*	Placeholder price (assumption)	Based on annual parity price to IV edaravone from CMS Payment Allowance Limit
Oral edaravone annual cost	$171,000	Redbook	Wholesale acquisition cost

*approximate price (based on exchange range from Canadian $ to US $) manufacturer used in submission to Canadian Agency for Drugs and Technologies in Health

Key Model Inputs: Health Care Sector-related Costs

	Recurring Monthly Costs*	Transitional Costs§
Stage 1	$668	$266
Stage 2	$1,647	$5,458
Stage 3	$2,314	$12,276
Stage 4a	$3,630	$42,598
Stage 4b	$3,630	$53,804

*costs for physician visits, outpatient facility, home healthcare, dietary supplements, cost of supplies for gastric tube and noninvasive ventilation, and medications other than ALS-specific drugs
§one-time fixed costs for durable medical equipment, gastric tube, and hospitalization

Key Model Inputs: Societal / Indirect Costs

	Recurring Monthly Costs*	Transitional Costs§
Stage 1	$1,371	$226
Stage 2	$3,721	$5,458
Stage 3	$5,485	$15,041
Stage 4a	$8,094	$59,260
Stage 4b	$8,094	$59,260
Death	$0	$7,586

*cost of absenteeism, informal/unpaid care, and transportation costs
§one-time fixed costs for home modification/moving, vehicle modification

Key Model Inputs: Utilities

Utility (King's stages)	Source	Notes
Stage 1: 0.65	Jones AR et al. 2014	Provided by persons with ALS in the UK who participated in a clinical trial using the EQ-5D
Stage 2: 0.53		
Stage 3: 0.41		
Stage 4a & 4b: 0.27		

Results

Base-Case Results for AMX0035

Drug	Drug Cost	Total Cost	LYs	QALYs	evLYs
AMX0035 + SOC (Multidisciplinary Care ± Riluzole ± IV Edaravone)	$380,000*	$569,000*	3.01	1.03	1.21
SOC alone	$105,000	$271,000	2.64	0.89	0.89

Drug	Comparator	Cost per QALY gained	Cost per evLY gained
AMX0035 + SOC (Multidisciplinary Care ± Riluzole ± IV Edaravone)	SOC alone	$2,136,000	$952,000

QALYs: quality-adjusted life years, evLYs: equal value of life years, LY: life year SOC: standard of care

*based on placeholder price

Base-Case Results for Oral Edaravone

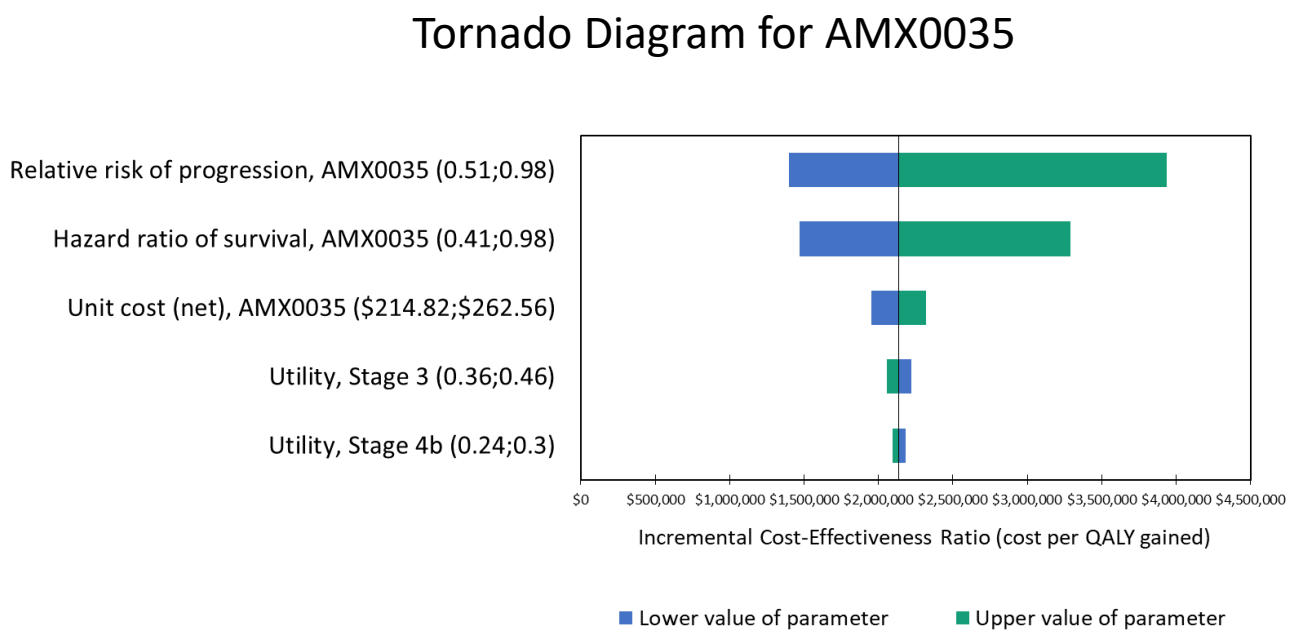
Drug	Drug Cost	Total Cost	LYs	QALYs	evLYs
Oral Edaravone + SOC (Multidisciplinary Care ± Riluzole)	$428,000	$598,000	2.70	0.93	0.94
SOC alone	$1,300	$166,000	2.64	0.89	0.89

Drug	Comparator	Cost per QALY gained	Cost per evLY gained
Oral Edaravone + SOC (Multidisciplinary Care ± Riluzole)	SOC alone	$11,981,000	$8,186,000

QALYs: quality-adjusted life years, evLYs: equal value of life years, LY: life year SOC: standard of care

*based on placeholder price

Sensitivity Analyses



- Probabilistic Sensitivity Analyses to calculate the proportion of simulations where AMX0035 and oral edaravone were cost-effective from $50,000/QALY to $150,000/QALY were 0%

Very High Background Costs

- In certain situations, when background health costs are very high, treatments that extend life may not be cost-effective at any price
- As a result, we excluded all background costs in our calculations to determine the Health Benefit Price Benchmarks (next slide) of AMX0035 and oral edaravone.

Health Benefit Price Benchmarks (HBPBs)

Annual Price Benchmarks for AMX0035 and oral edaravone

Intervention	Annual WAC	Health Benefit Price Benchmark (include footnote based on range)	Discount from WAC to Reach Threshold Prices
AMX0035	$169,000*	$9,100 - $30,600*	81.9%-94.6%*
Oral edaravone	$171,000	$1,400 - $3,200	98.1%-99.2%

WAC: wholesale acquisition cost
*based on placeholder price

Scenario Analyses

- Modified societal analysis
  - Similar results as the base case for both AMX0035 and oral edaravone
- None of the other scenarios had a substantial impact on the conclusions

Limitations

- Placeholder price for AMX0035
- Lack of evidence on treatment effect heterogeneity
- Lack of evidence on within King's stage treatment effect

Comments Received

- Edaravone patient population and efficacy
- Updated parameters on AMX0035 survival
- Use of King's staging vs. other model schematics

Conclusions

- AMX0035 and oral edaravone provide clinical benefit in terms of gains in QALYs, LYs, and evLYs over their respective SOC alone
- If priced similarly to the assumed placeholder price, AMX0035 would not meet commonly cited cost-effectiveness thresholds
- At its current price, oral edaravone does not meet commonly cited cost-effectiveness thresholds

Questions?

Manufacturer Public Comment and Discussion

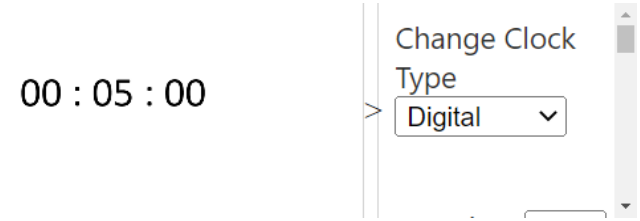
Manufacturer Public Commenters

Speaker	Title	Affiliation
Stephen Apple, MD	Executive Medical Director, Medical Affairs	Mitsubishi Tanabe Pharma America, Inc.

Stephen Apple, MD, Executive Medical Director, Medical Affairs
Mitsubishi Tanabe Pharma America, Inc.

Conflicts of Interest:

- *Dr. Apple is a full-time employee of Mitsubishi Tanabe Pharma America, Inc.*

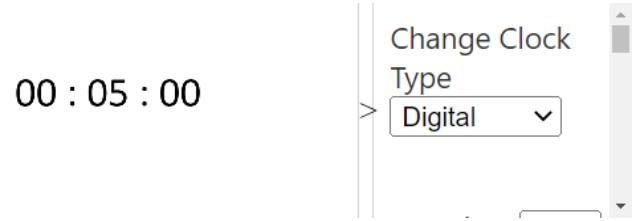


Public Comment and Discussion

Benjamin Rix Brooks, MD, Director
Clinical Trials Planning LLC

Conflicts of Interest:

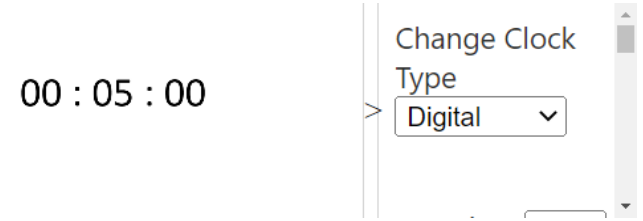
- *Dr. Brooks receives funding and research support from Mitsubishi Tanabe Pharma America.*



Steve Kowalski
Person Living with ALS

Conflicts of Interest:

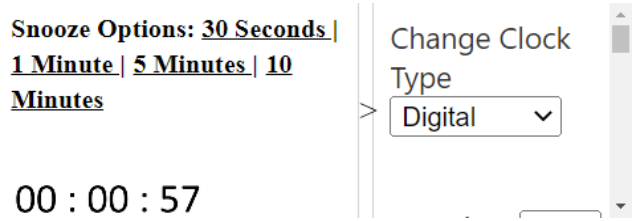
- *No conflicts of interest to disclose.*



Sunny Brous
Person Living with ALS

Conflicts of Interest:

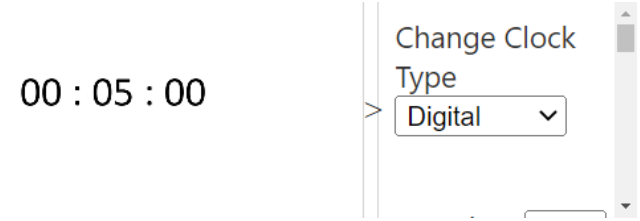
- *Sunny has prepared oral comments in collaboration with the ALS Association.*



Scott Kaufman, MBA, Chairman
The ALS Association

Conflicts of Interest:

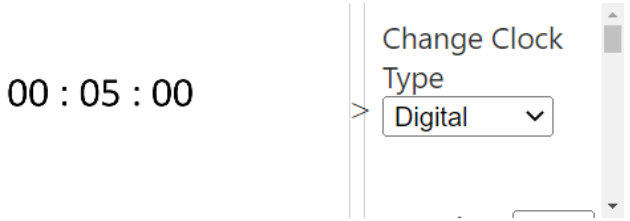
- *The ALS Association has provided Amylyx with a $750,000 grant for a clinical trial pilot, and the Association has provided the Northeast ALS Consortium (NEALS) with a $1.46 million grant to help pay for the phase 2 clinical trial of AMX0035. As a standard provision in philanthropic support for drug development, the grants to Amylyx and for the clinical trial of AMX0035 included repayment provisions allowing the Association to recover up to 150 percent of its support, or up to $3.3 million. Any funds received will be reinvested into ongoing global research into treatments and cures.*



Calaneet Balas, MS, MBA, President and CEO
The ALS Association

Conflicts of Interest:

- *The ALS Association has provided Amylyx with a $750,000 grant for a clinical trial pilot, and the Association has provided the Northeast ALS Consortium (NEALS) with a $1.46 million grant to help pay for the phase 2 clinical trial of AMX0035. As a standard provision in philanthropic support for drug development, the grants to Amylyx and for the clinical trial of AMX0035 included repayment provisions allowing the Association to recover up to 150 percent of its support, or up to $3.3 million. Any funds received will be reinvested into ongoing global research into treatments and cures.*



Lunch

Meeting will resume at 12:00pm

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Voting Questions

Clinical Evidence

Patient Population for all questions (unless otherwise specified): Adult person with ALS.

1. Is the evidence adequate to demonstrate that the net health benefit of AMX0035 plus standard of care is superior to that provided by standard of care alone (i.e., multidisciplinary care that may involve treatment with riluzole and/or IV edaravone)?

A. Yes

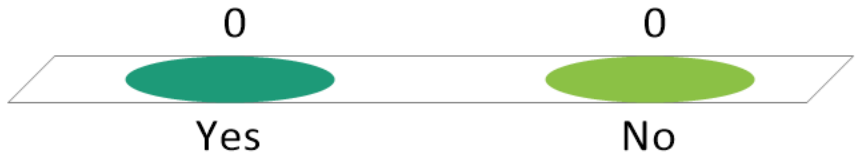
B. No

Patient population for question 2: *Adults with ALS who meet the narrow Study 19 criteria*

2. Is the evidence adequate to demonstrate that the net health benefit of oral edaravone plus standard of care is superior to that provided by standard of care alone (i.e., multidisciplinary care that may involve treatment with riluzole)?

A. Yes

B. No

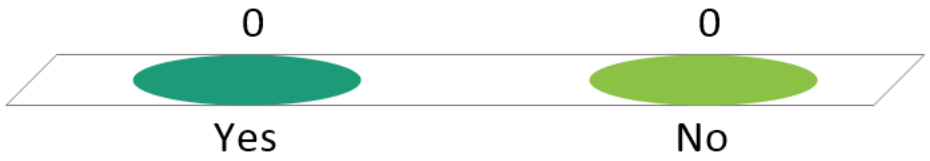


Patient population for question 3: *Adults with ALS who do not meet Study 19 criteria*

3. Is the evidence adequate to demonstrate that the net health benefit of oral edaravone plus standard of care is superior to that provided by standard of care alone (i.e., multidisciplinary care that may involve treatment with riluzole)?

A. Yes

B. No



Contextual Considerations and Potential Other Benefits or Disadvantages

When making judgments of overall long-term value for money, what is the relative priority that should be given to any effective treatment for ALS, on the basis of the following contextual considerations:

1. Acuity of need for treatment of individual patients based on short-term risk of death or progression to permanent disability

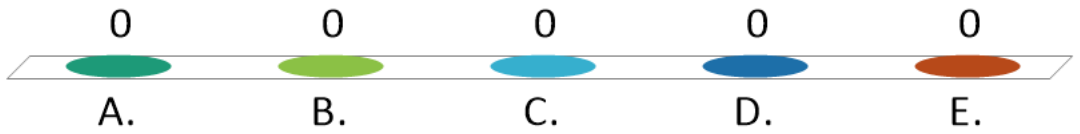
A. Very low priority

B. Low priority

C. Average priority

D. High priority

E. Very high priority



2. Magnitude of the lifetime impact on individual patients of the condition being treated

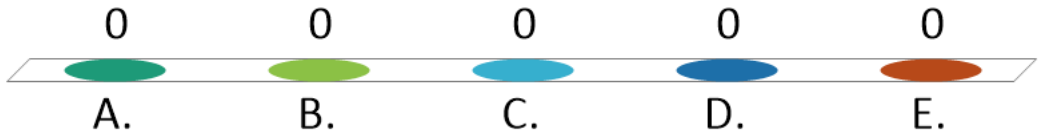
A. Very low priority

B. Low priority

C. Average priority

D. High priority

E. Very high priority



What are the relative effects of AMX0035 plus standard of care versus standard of care alone on the following outcomes that inform judgment of the overall long-term value for money of AMX0035?

3. Patients' ability to achieve major life goals related to education, work, or family life

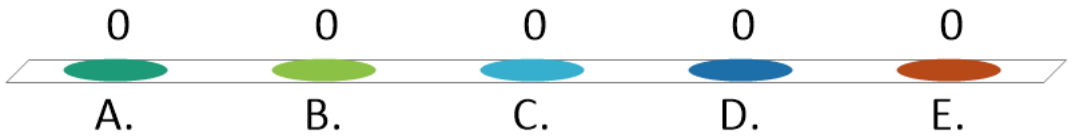
A. Major negative effect

B. Minor negative effect

C. No difference

D. Minor positive effect

E. Major positive effect



4. Caregivers' quality of life and/or ability to achieve major life goals related to education, work, or family life

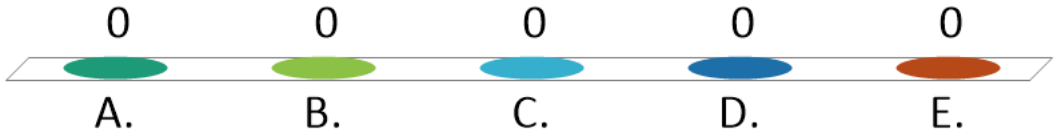
A. Major negative effect

B. Minor negative effect

C. No difference

D. Minor positive effect

E. Major positive effect



What are the relative effects of oral edaravone plus standard of care versus standard of care alone on the following outcomes that inform judgment of the overall long-term value for money of oral edaravone?

5. Patients' ability to achieve major life goals related to education, work, or family life

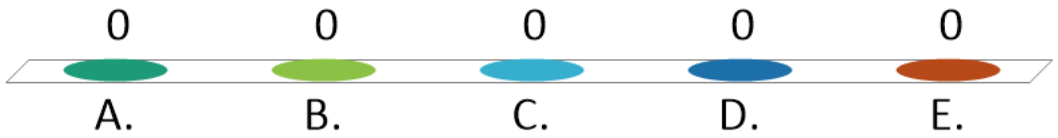
A. Major negative effect

B. Minor negative effect

C. No difference

D. Minor positive effect

E. Major positive effect



6. Caregivers' quality of life and/or ability to achieve major life goals related to education, work, or family life

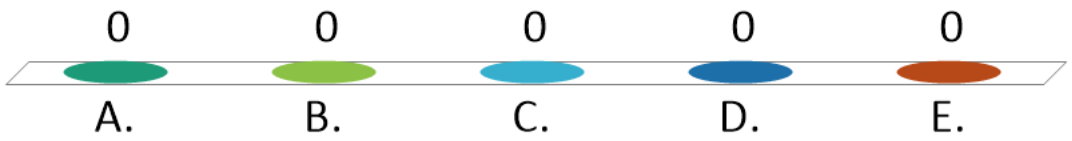
A. Major negative effect

B. Minor negative effect

C. No difference

D. Minor positive effect

E. Major positive effect



7. Patients' ability to manage and sustain treatment given the complexity of regimen compared to IV edaravone

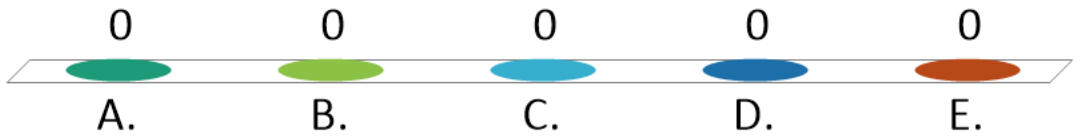
A. Major negative effect

B. Minor negative effect

C. No difference

D. Minor positive effect

E. Major positive effect



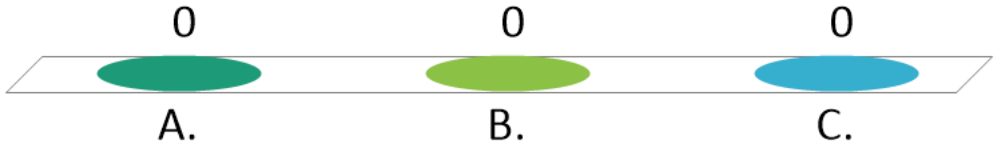
Long-term Value for Money

1. Given the available evidence on comparative effectiveness and incremental cost-effectiveness, and considering other benefits, disadvantages, and contextual considerations, what is the long-term value for money of treatment with AMX0035 at its proposed price in Canada (USD 169,000) compared to usual care alone (i.e., multidisciplinary care that may involve treatment with riluzole and/or IV edaravone)?

A. Low long-term value for money at assumed pricing

B. Intermediate long-term value for money at assumed pricing

C. High long-term value for money at assumed pricing

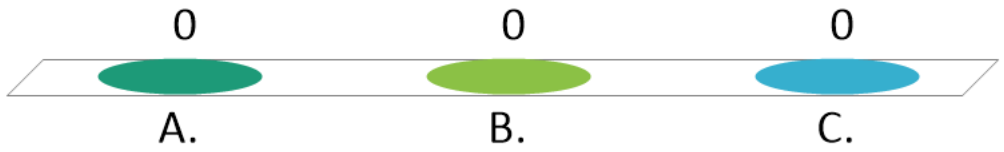


2. Given the available evidence on comparative effectiveness and incremental cost-effectiveness, and considering other benefits, disadvantages, and contextual considerations, what is the long-term value for money of treatment of oral edaravone, at current pricing, compared to usual care alone (i.e., multidisciplinary care that may involve treatment with riluzole)?

A. Low long-term value for money at assumed pricing

B. Intermediate long-term value for money at assumed pricing

C. High long-term value for money at assumed pricing



Break

Meeting will resume at 2:00pm

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Policy Roundtable

Policy Roundtable

Policy Roundtable Participant	Conflict of Interest
Stephen Apple, MD, Executive Medical Director, Medical Affairs, Mitsubishi Tanabe Pharma America, Inc.	Dr. Apple is a full-time employee of Mitsubishi Tanabe Pharma America, Inc.
Richard Bedlack, MD, PhD, Professor of Neurology, Director of ALS Clinic, Duke University School of Medicine	Dr. Bedlack has received consulting support in excess of $5,000 and research support from the ALS Association and Amylyx.
Mary Catherine Collet, MS, ALS Patient Advocate	Ms. Collet is a past employee of Eli Lilly and received a vested pension benefit. She also owns more than $10,000 in Eli Lilly shares.
Aaron Lewis, MD, Neurologist, Neuromuscular Medical Director, ALS Multidisciplinary Clinic, Kaiser Permanente	Dr. Lewis has received a grant from the ALS Association in support of patient care.
Michelle Rogers, PharmD, BCPS, Director of Clinical Pharmacy, IPD Analytics	Dr. Rogers is a full-time employee of IPD Analytics.
Joel Shamaskin, MD, Person with ALS; Professor Emeritus of Medicine (Retired), University of Rochester School of Medicine and Dentistry	No relevant conflicts of interest to disclose, defined as more than $10,000 in health care company stock or more than $5,000 in honoraria or consultancies during the previous year from health care manufacturers or insurers. Dr. Shamaskin serves on the ALS Association research committee.
Emily Tsiao, PharmD, Clinical Pharmacist, Utilization Management, Premera Blue Cross	Dr. Tsiao is a full-time employee of Premera Blue Cross.

Midwest CEPAC Council Reflections

Next Steps

- Meeting recording posted to ICER website next week
- Final Report published on or around September 19th, 2022
- Includes description of Midwest CEPAC votes, deliberation, policy roundtable discussion
- Materials available at: https://icer.org/assessment/amyotrophic-lateral-sclerosis-2022/#timeline

Adjourn

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