Tolebrutinib for Secondary Progressive Multiple Sclerosis: Effectiveness and Value

Public Meeting — June 13, 2025

Meeting materials available at: https://icer.org/assessment/multiple-sclerosis-2025/

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CTAF
CALIFORNIA TECHNOLOGY ASSESSMENT FORUM

Patient Experts

Kathleen Costello, CRNP, MSCN, Interim CEO, Consortium of MS Centers

- *The Consortium of MS Centers and Can Do MS receive sponsorships and educational grants from the following Pharmaceutical Companies: Amgen, Biogen, EMD Serono, Bristol Myers Squibb, Genentech, Kyverna, Novartis, Sandoz, Sanofi, Octave Bioscience, TG Therapeutics, Vanda and Viatris. Kathleen Costello has no personal disclosures.*

Nancy Garcia, MTS, BCC, Retired Chaplain, Patient

- *No conflicts to disclose.*

Clinical Experts

Robert Bermel, MD, MBA, FAAN, Director, Mellen Center for Multiple Sclerosis, Cleveland Clinic

- *Dr. Bermel has served as a consultant for Genzyme/Sanofi, Genentech/Roche, Novartis, and TG Therapeutics and received consulting fees in excess of $5,000. He also serves as a volunteer member of the Medical Advisory Board, which has received >25% of its funding from healthcare companies.*

Ellen Mowry, MD, MCR, Professor of Neurology & Epidemiology, Johns Hopkins University

- *Johns Hopkins University has received funding from Roche/Genentech and Biogen.*

ICER Speakers

Sarah K. Emond, MPP
President & CEO

Grace Lin, MD
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Medical Director for HTA, ICER

Foluso Agboola, MBBS, MPH
Senior Vice President of Research, ICER

Brett McQueen, PhD
Associate Professor, University of Colorado Anschutz Medical Campus

Why are we here today?

“It’s been a long journey... I started with a cane, which became a walker, which became a rollator, which was replaced by a small electrical foldable wheelchair… I mostly talk to my computer. I don’t attempt to type anymore.”

“I mean, it’s very hard not to be in a completely depressed place, because I just feel like unless someone comes through with something truly novel, I’ve done really all the drugs that are out there.”

“I think balance is a big one for me, and fatigue…I have an identical twin sister, so it’s a very good way of seeing how much my life is impacted. You know, she does a lot more than I do….you try to do thing, and you just don’t have the wherewithal.”

Patients living with MS

Why Are We Here Today?

- What happens the day these treatments receive FDA approval?
- Questions about:
  - 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

DIAGNOSIS: DEBT

100 Million People in America Are Saddled With Health Care Debt

By Noam N. Levey

JUNE 16, 2022

Why Delaware is eying a 27% premium hike on state employees' health insurance

Amanda Fries

Delaware News Journal

Published 4:35 a.m. ET Feb. 1, 2024 | **Updated 9:29 p.m. ET Feb. 6, 2024**

NBER

National Bureau of Economic Research

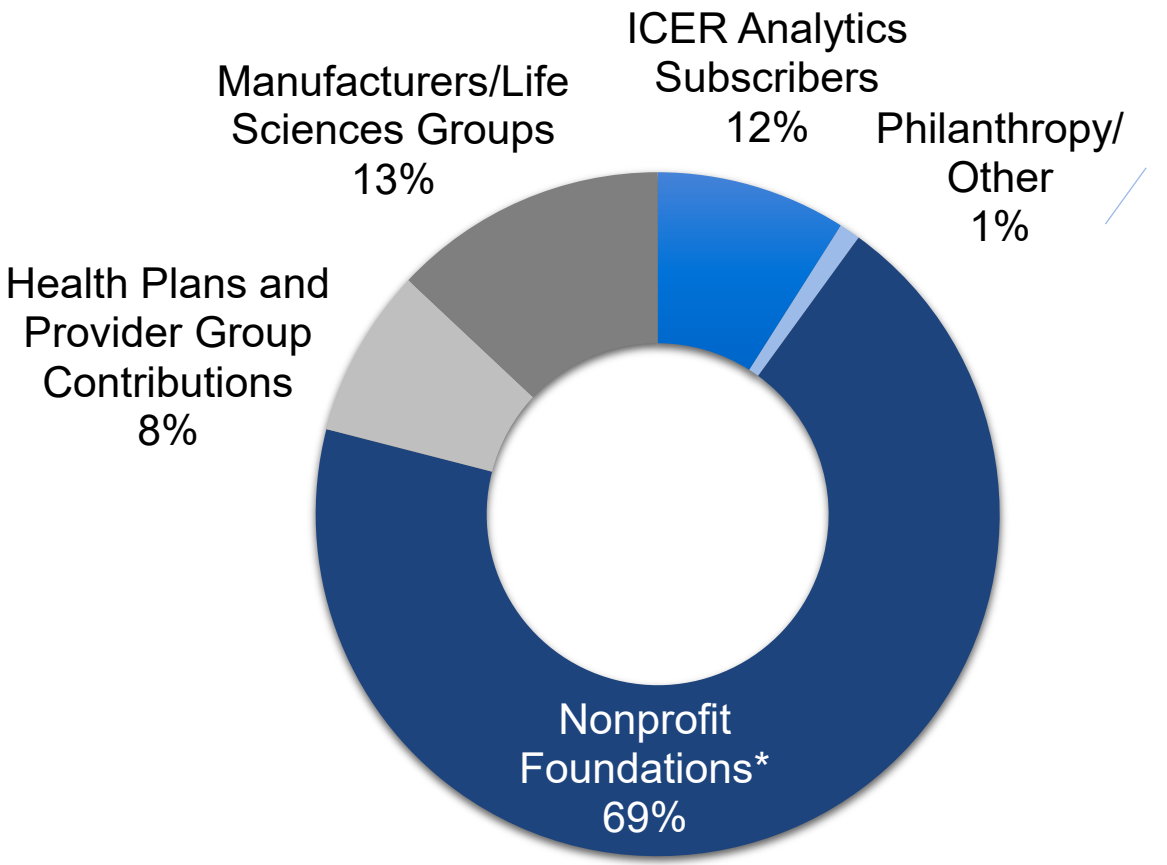
WHO PAYS FOR RISING HEALTH CARE PRICES?

100 Million People in America Are Saddled With Health Care Debt (KFF Health News)

Why Delaware is eying a 27% premium hike on state employees' health insurance (Delaware Online)

Organizational Overview

2025 Funding and Managing COIs



Read our policies to manage potential conflicts of interest: https://icer.org/our-approach/policies/policies-to-manage-conflicts-of-interest/

ICER Policy Summit and non-report activities only

*ICER received significant funding from Arnold Ventures, The California Health Care Foundation, The Patrick and Catherine Weldon Donaghue Medical Research Foundation, and the Peterson Center on Healthcare, LLC.
Source: https://icer.org/who-we-are/independent-funding/sources-of-funding/

How Was the ICER Report Developed?

Guidance from patients, clinical experts, manufacturers, and other stakeholders

Evidence analysis in collaboration with the University of California San Francisco and cost-effectiveness modeling in collaboration with the University of Colorado

- **Bruce A. Cohen, MD,** Professor of Neurology, Northwestern University, Feinberg School of Medicine, Davee Department of Neurology
- **Kavita V. Nair, PhD,** Professor of Neurology and Pharmacy, University of Colorado Anschutz Medical Campus
- **Hollie Schmidt, MS, MBA,** Vice President of Scientific Operations, Accelerated Cure Project for MS
- **Simone Huygens, PhD,** Health Economist, Huygens & Versteegh
- **Matthijs Versteegh, PhD, MA, BSc,** HTA Specialist, Huygens & Versteegh; Dutch Health Care Institute

Structured to support **CTAF** voting and policy discussion

Value Assessment Framework: Long-Term Value for Money

Agenda (PT)

9:00 AM	Meeting Convened and Opening Remarks
9:20 AM	Presentation of the Clinical Evidence
10:00 AM	Presentation of the Economic Model
10:40 AM	Public Comments and Discussion
11:00 AM	Lunch Break
11:50 AM	CTAF Deliberation and Vote
12:50 PM	Break
1:00 PM	Policy Roundtable Discussion
2:30 PM	Reflections from CTAF
3:00 PM	Meeting Adjourned

Presentation of the Clinical Evidence

Grace Lin, MD, MAS

Medical Director for Health Technology Assessment, ICER

Professor of Medicine, UCSF

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Key Team Members

Name	Title
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Finn Raymond	Research Assistant II, Evidence Synthesis

Disclosures

Financial support provided to UCSF and Dr. Lin from the Institute for Clinical and Economic Review (ICER).

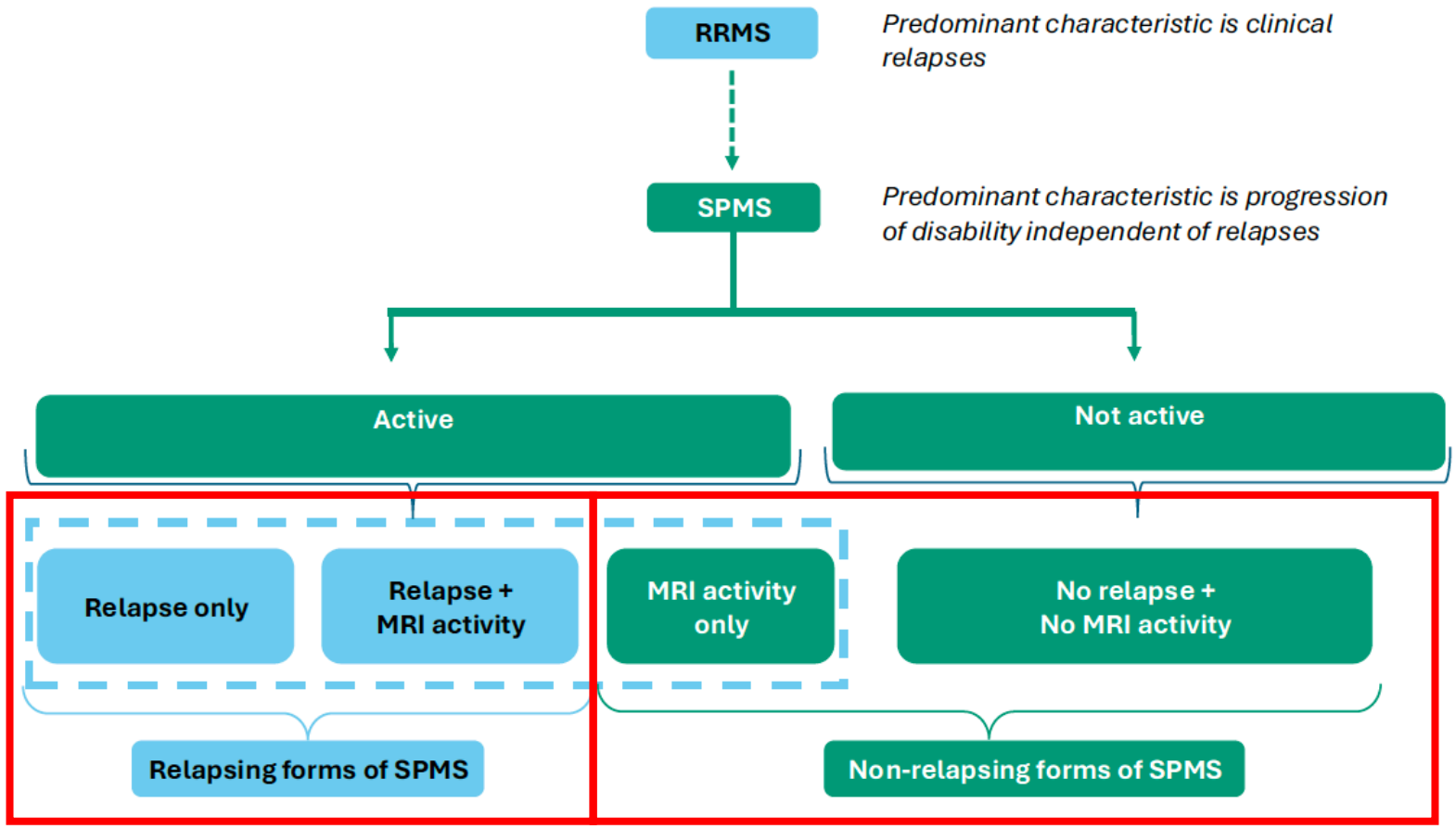
Dr. Lin, Dr. Fahim, and Mr. Raymond have no conflicts to disclose.

Multiple Sclerosis (MS)

Disease Background

- Inflammatory disease that damages myelin sheath, leading to progressive deterioration of axons
- Affects nearly 1 million Americans
  - Women more than men
  - Age 45-65 most affected
- Racial and ethnic disparities
  - Black persons in US have higher incidence of disease, more rapid disease progression, and greater disability
  - Onset of disease appears earlier in Hispanic persons born in US
- Most people with MS start out with relapsing-remitting MS (RRMS), then over 3-4 decades progress to secondary progressive MS (SPMS)

Categories of SPMS



Symptom Chart

Symptom

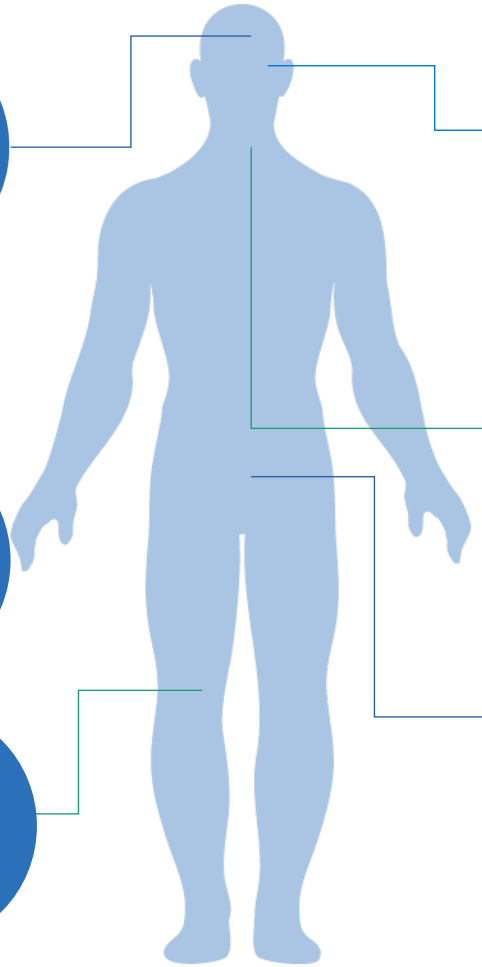
Numbness
Weakness
Cognitive and mood changes
Poor balance and coordination

Symptom

Fatigue
Pain

Symptom

Muscle cramps/spasm



Symptom

Vision changes

Symptom

Difficulty swallowing

Symptom

Bowel and bladder incontinence

Impact on Patients

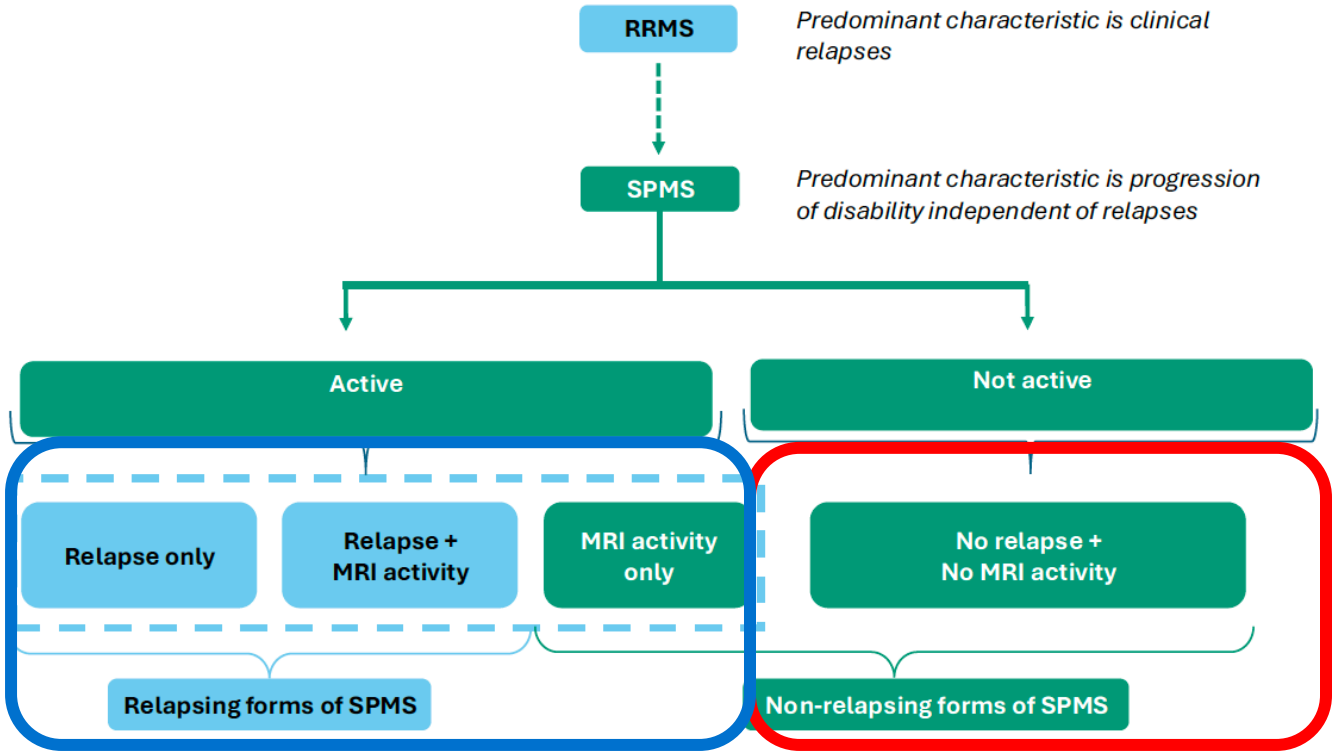
- MS has large impact on physical health, mental health, work/educational productivity, family planning, leisure activities
- Both initial diagnosis and transition to SPMS may be delayed
- Some symptoms not adequately treated by disease-modifying therapies (DMT)
- Access to specialist care and coordination of care an be difficult, particularly in rural areas
- High caregiver burden
- Older patients afraid they may not be treated as aggressively

Impact on Patients – Survey of MS Patients

- Persons living with SPMS reported substantial mobility impairment
- Slowing of progression is an important goal but also would like to see drugs aimed at clinical improvement, remyelination
- 15% of persons living with MS reported delays in treatment due to financial barriers
  - More than 40% receive financial assistance for medication

Standard of Care and Management for Non-relapsing SPMS

- For active SPMS (still having relapses), standard of care is DMT + supportive care
- For non-active SPMS, no current drug therapies are approved



Scope of Review

- To assess the clinical effectiveness of tolebrutinib compared with usual care in persons living with non-relapsing forms of SPMS

Tolebrutinib

- Bruton's tyrosine kinase inhibitor (BTKI).
- Modulates persistent activation of BTK enzyme in central nervous system, thought to decrease neuroinflammation.
- Once daily oral medication, 60 mg dose.
- Studied in relapsing (GEMINI 1&2) and non-relapsing forms of MS (HERCULES); separately being studied for PPMS (PERSEUS).
- New drug application filed for non-relapsing forms of MS, decision expected by September 2025.

Clinical Evidence

Pivotal Trial: HERCULES

Study Design

- Phase III, randomized 2:1, double-blind, placebo-controlled study
- Diagnosis of non-relapsing SPMS
- EDSS 3 to 6.5
- No clinical relapse in last 24 months
- Documented disability progression in last 12 months

Baseline Characteristics

- 1131 participants
- Mean age: 49 years
- Mean EDSS: 5.5-5.6
- ~62% Female, 93% White
- Mean ~7.5-8 yrs from SPMS diagnosis and last clinical relapse
- 13% showed MRI disease activity (active SPMS)

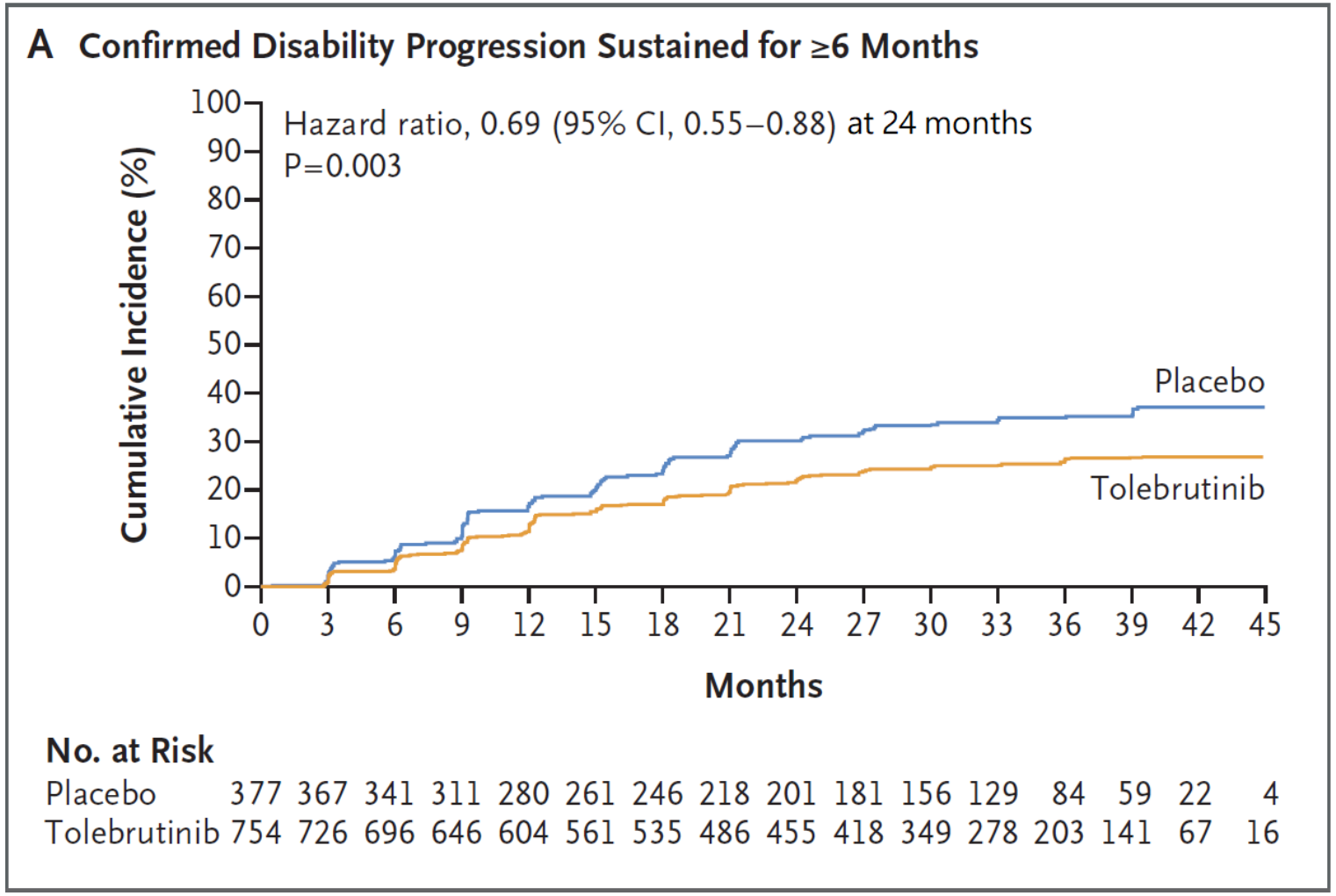
EDSS: Expanded Disability Status Scale, mg: milligram, MRI: magnetic resonance imaging, SPMS: secondary progressive multiple sclerosis

Outcomes

- Primary outcome: Time to 6-month confirmed disability progression (CDP)
- Six hierarchical secondary outcomes:
  - Time to 3-month CDP
  - Number of new or enlarging T2 lesions per year
  - Time to sustained 20% worsening in 9-HPT score for ≥3 months
  - Time to sustained 20% worsening in T25FWT score for ≥3 months
  - Time to 6-month confirmed disability improvement (CDI)
  - Percent change in brain volume

CDI: confirmed disability improvement, CDP: confirmed disability progression, 9-HPT: 9-hole peg test, T25FWT: timed 25-foot walk test

Primary Endpoint: Time to 6-Month CDP



Source: Data from Fox et al 2025

Disability Progression and Improvement-Related Outcomes

Baseline Characteristic	Tolebrutinib (N = 754)	Placebo (N = 377)	Between-Group Difference at 24 Months; HR (95% CI)	P Value
Proportion of Patients Achieving 6-month CDP	22.6%	30.7%	0.69 (0.55 to 0.88)	**P = 0.003**
Proportion of Patients Achieving >20% Worsening in 9-HPT score	19%	19.6%	0.97 (0.74 to 1.29)	P = 0.84
Proportion of Patients Achieving >20% Worsening in T25FWT score	41.1%	49.6%	0.77 (0.64 to 0.92)	NR
Proportion of Patients Achieving 6-month CDI	8.6%	4.5%	1.88 (1.10 to 3.21)	NR

CI: confidence interval, CDI: confirmed disability improvement, CDP: confirmed disability progression, HR: hazard ratio, NR: significance testing not reported due to prespecified hierarchical sequence, 9-HPT: 9-hole peg test, T25FWT: timed 25-foot walk test

MRI Outcomes

Baseline Characteristic	Tolebrutinib (N = 754)	Placebo (N = 377)	Between-Group Difference at 24 Months; (95% CI)	P Value
Annualized New or Enlarging T2 Lesions Rate: Mean estimate (95% CI)	1.84 (1.44 to 2.34)	2.95 (2.24 to 3.88)	RR: 0.62 (0.43 to 0.90)	**P = 0.01**
Percentage Change in Brain Volume Loss: Mean Change (SE)	-0.69% (0.03)	-0.78% (0.05)	MD: 0.08 (-0.03 to 0.20)	NR

CI: confidence interval, MD: mean difference; NR: significance testing not reported due to prespecified hierarchical sequence; RR: relative risk, SE: standard error

Key Harms

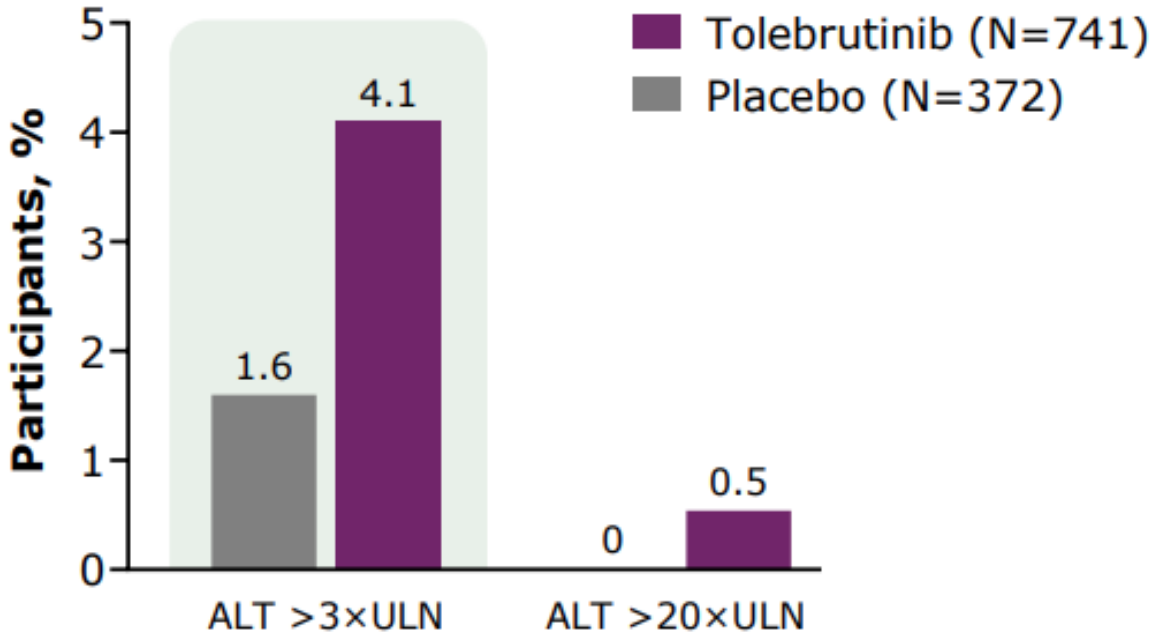
Overall

- High rates of discontinuation (23%)
- AE-related discontinuations: 4% in tolebrutinib vs. 3% in placebo
- Serious AEs: 15% in tolebrutinib vs. 10% in placebo
- Two deaths in tolebrutinib group vs. one in placebo, one deemed related to the drug
- Most common AEs: nasopharyngitis, fall, headache, infections (e.g., COVID-19, respiratory, urinary)

AE: adverse event, ULN: upper limit of the normal

Liver Toxicity

- 4.1% LFT elevation > 3x upper limit of normal (ULN)
- 4 total cases (0.5%) of severe liver toxicity (ALT > 20x ULN), including one death
  - 1 case after protocol change
- Monitoring after protocol change:
  - Week 2 to 12: weekly
  - Months 3 to 12: monthly
  - Until study completion: quarterly



Source: Data from Fox et al 2025;
ALT: alanine aminotransferase; ULN: upper limit of normal

Controversies and Uncertainties

Key Points

- Mixed results on secondary endpoints – e.g., brain volume loss
- No data on patient-important outcomes (e.g., HRQoL, cognitive function)
- Only a few patients achieved disability improvement
- Potential unblinding due to increased liver monitoring
- New mechanism of action with no long-term safety data
- No data on subgroups (i.e., active and non-active forms of SPMS)

Benefits Beyond Health and Special Ethical Priorities

Key Points

- Substantial unmet need – no treatments currently approved for non-active SPMS
- Black Americans living with MS have a higher incidence of disease, more rapid disease progression, and greater disability
- Slowing of progression may decrease caregiver burden
- Oral administration may improve access in some cases

Public Comments Received

- Elevation in liver function tests were mitigated by implementation of a more intensive monitoring program
  - Adherence to intensive liver function test monitoring may be difficult in real world practice

Summary

- Tolebrutinib slows progression of disability (6-month CDP) in persons living with SPMS.
  - Mixed data on secondary outcomes
  - Treatment could possibly lead to disability improvement in a small number of people
- There remains a risk of severe hepatotoxicity.
  - Intense monitoring may not be feasible to fully implement in real-world practice
- However, given the lack of current treatment options for non-relapsing forms of SPMS, tolebrutinib could help fill an important gap in care.

ICER Evidence Ratings for Tolebrutinib

Treatment	Comparator	Population	Evidence Rating
Tolebrutinib	Best supportive care	Non-Relapsing SPMS	P/I (promising but inconclusive)

P/I: Moderate certainty of a small or substantial net health benefit, small likelihood of a negative net health benefit

Questions?

Presentation of the Economic Model

R. Brett McQueen, PhD

Associate Professor, University of Colorado Anschutz Medical Campus

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Key Team Members

Name	Title
Brett McQueen	Lead modeler, Associate Professor, CU
Antal Zemplenyi	Modeler, Visiting Research Professor, CU
Marina Richardson	Associate Director, HTA Methods and Health Economics, ICER
Marie Phillips	Health Economics Research Assistant, ICER

Disclosures

Financial support provided to the University of Colorado from the Institute for Clinical and Economic Review (ICER).

RBM reports compensation from Sanofi for a special speaker series in April 2024 related to type 1 diabetes and fees for reviewing a project attempting to improve early diagnosis of type 1 diabetes. He has not received any funding directly related to a product or directly related to multiple sclerosis.

Objective

To evaluate the lifetime cost-effectiveness of Tolebrutinib compared to best supportive care for the treatment of non-relapsing Secondary Progressive Multiple Sclerosis (SPMS).

Unmet Need

Condition	Absolute evLY Shortfall	Proportional evLY Shortfall
Secondary Progressive MS	18.3	64%
Other Example Conditions		
Chronic Kidney Disease	18.1	79%
Amyotrophic Lateral Sclerosis	19.4	95%
Osteoporosis	2.6	19%

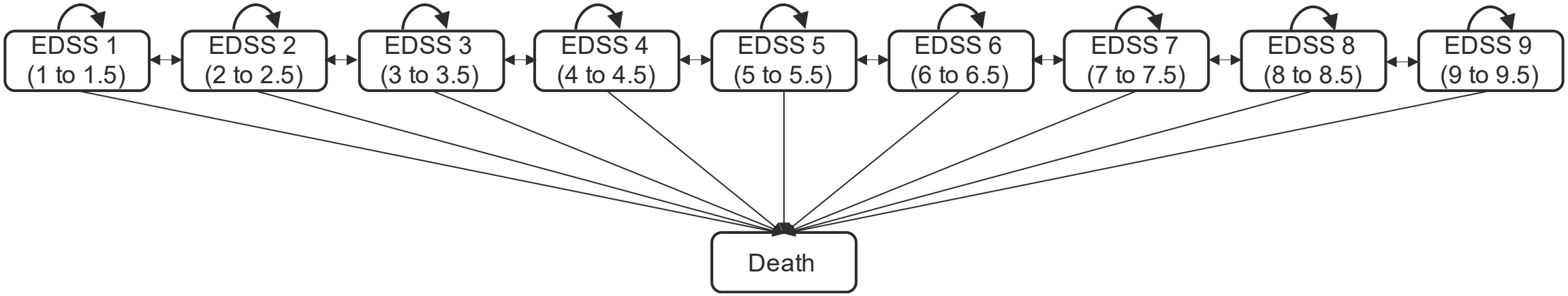
Methods in Brief

Methods Overview

Domain	Approach
Model	Markov model
Setting	United States
Perspective	Health Care Sector Perspective and Modified Societal Perspective
Time Horizon	Patient lifetime
Discount Rate	3% per year (costs and outcomes)
Cycle Length	Annual
Primary Outcome	Incremental and total life years gained, QALYs, evLY; clinical outcome of years able to walk without a wheelchair (EDSS <7)

evLY: equal value of life years gained, QALY: quality-adjusted life years

Model Schematic



In the base-case analysis, no patients transitioned to and from EDSS 9, consistent with the placebo and tolebrutinib arms of the HERCULES trial. The health states are categorized into whole unit increments based on the EDSS. Transitions occur annually.

Model Characteristics

Baseline Characteristic	Tolebrutinib (N=754)	Placebo (N=377)	Source
Age, Mean (SD)	48.9 (8.0)	48.9 (8.0)	Fox et al., 2025
Female, n (%)	454 (60.2)	242 (64.2)	
EDSS, Mean (SD)	5.5 (1.0)	5.6 (0.9)	

EDSS: Expanded Disability Status Scale, SD: standard deviation

Key Assumptions

Assumption 1

- In the base-case analysis, no patients transitioned to and from EDSS 9, consistent with the placebo and tolebrutinib arms of the HERCULES trial.

Assumption 2

- EDSS transitions will follow the minimum confirmed disability progression (CDP) criteria from the HERCULES trial: 1.0-point increase for baseline EDSS ≤5.0, 0.5 for >5.0.

Assumption 3

- Six-month confirmed disability improvement (CDI) was not considered in the base-case model as it does not necessarily represent a true reversal of disease progression.

SPMS Disease Transition Options

- Base-case uses contemporary SPMS transitions provided by the manufacturer.
  - Limited follow-up with no transitions through EDSS 9 but progression and improvement in both arms of the model
- Scenario analysis uses a historical cohort (15+ years ago) of SPMS patients from London, Ontario with progression across EDSS 1 – 9.

Key Model Inputs: Efficacy

Disability Progression

	Proportion of Patients Achieving 6-Month Disability Progression at 24 Months	Hazard Ratio for 6-Month Disability Progression (CI)	Primary Source
Tolebrutinib	22.6%	0.69 (0.55 to 0.88)	Fox et al., 2025
Placebo	30.7%	NA	

Disability Improvement (Scenario Analysis Only)

	Proportion of Patients Achieving 6-Month Disability Improvement at 24 Months	Hazard Ratio for 6-Month Disability Improvement (CI)	Primary Source
Tolebrutinib	8.6%	1.88 (1.10, 3.21)	Fox et al., 2025
Placebo	4.5%	NA	

CI: confidence interval

Treatment and Monitoring Costs

Drug Cost

Intervention	Annual Placeholder WAC	Source
Tolebrutinib	$115,000	IPD Analytics

Drug Monitoring Unit Costs

Category	Unit Cost	Source
MRI (CPT 70543), every 6-mo	$473	Physician Schedule Fee, 2024
Provider Visit (CPT 99215), every 3-mo	$175	
Liver Function Test (HCPCS 80076)	$62	

CPT: Current Procedural Terminology, WAC: Wholesale Acquisition Cost

MS-Related Non-Drug Costs

EDSS State	Annual Cost	Source
EDSS 1	$10,808	Kobelt et al., 2006; Bebo et al., 2022 (from ICER 2023 Review; inflated to 2024 USD)
EDSS 2	$15,330	
EDSS 3	$19,848	
EDSS 4	$24,367	
EDSS 5	$28,889	
EDSS 6	$33,410	
EDSS 7	$37,929	
EDSS 8	$42,448	
EDSS 9*	$46,969	

*EDSS 9 standardized mortality ratio, utilities, and health care costs were only included in the scenario analysis using the London Ontario Cohort data.

Health State Utilities

EDSS State	Utility	Source
EDSS 1	0.7905	Mauskopf et al., 2016 and ICER MS Review 2023
EDSS 2	0.7365	
EDSS 3	0.6509	
EDSS 4	0.5816	
EDSS 5	0.5005	
EDSS 6	0.4118	
EDSS 7	0.3000	
EDSS 8	0.1482	
EDSS 9*	0.0485	

*EDSS 9 standardized mortality ratio, utilities, and health care costs were only included in the scenario analysis using the London Ontario Cohort data.

Mortality

EDSS State	Base Case SMR	Source
EDSS 1	1.43 (1.16-1.72)	Pokorski et al., 1997
EDSS 2	1.6 (1.28-1.92)	
EDSS 3	1.64 (1.31-1.96)	
EDSS 4	1.67 (1.34-2.01)	
EDSS 5	1.84 (1.47-2.21)	
EDSS 6	2.27 (1.82-2.73)	
EDSS 7	3.1 (2.48-3.72)	
EDSS 8	4.45 (3.56-5.34)	
EDSS 9*	6.45 (5.16-7.74)	

*EDSS 9 standardized mortality ratio, utilities, and health care costs were only included in the scenario analysis using the London Ontario Cohort data.

Modified Societal Perspective

- Indirect costs based on EDSS state inclusive of productivity losses, changes in labor employment participation, and informal care.
  - Range from $13,000 (EDSS 1) up to $42,000 (EDSS 9) annually
- Caregiver disutility
  - Range from no change (EDSS 1) to a maximum of -0.167 (EDSS 6)

Results

Discounted Base-Case Results

Treatment	Intervention Acquisition Costs*	Intervention-Related Costs†	Non-Intervention Related Costs‡§	Total Costs*§	QALYs	evLYs	Life Years	Years Without a Wheelchair (EDSS <7)§
Tolebrutinib	$1,821,000	$11,000	$672,000	$2,504,000	7.36	7.46	16.44	14.33
Best Supportive Care	$0	$0	$686,000	$686,000	6.83	6.83	16.18	13.09

*Based on placeholder price

†Intervention-related costs include costs of monitoring required for the intervention, as specified in clinical trials, guidelines, or package label

‡Non-intervention related costs include health state costs related and unrelated to SPMS and cost of death

§ Slight changes to the results have been made in between the report posting and the presentation of these results that will be reflected in the final evidence report

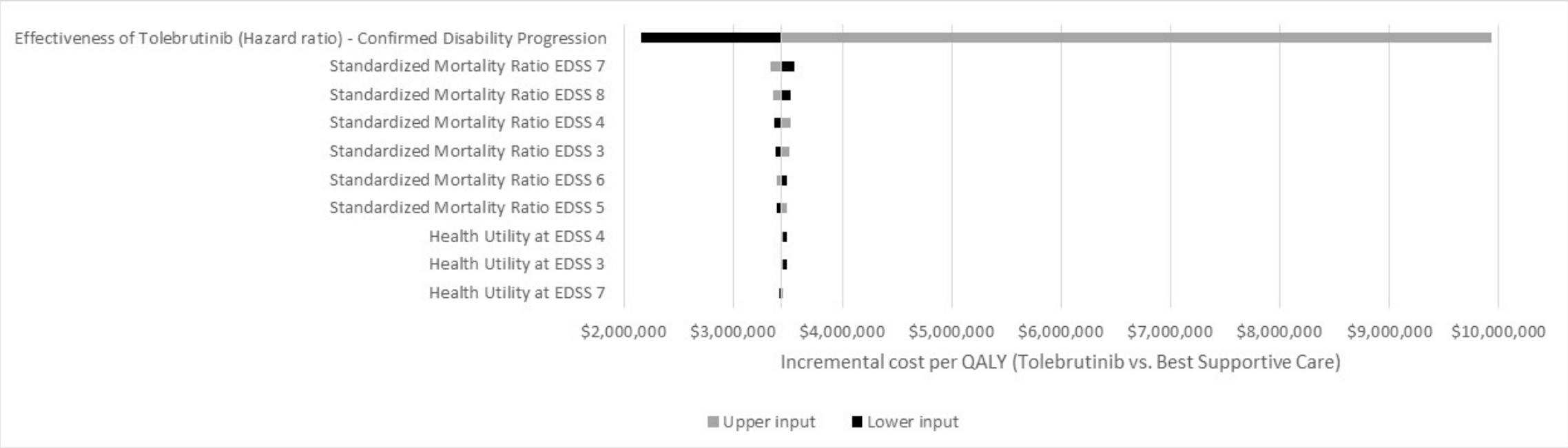
Discounted Base-Case Incremental Results

Treatment	Comparator	Cost per QALY Gained*	Cost per evLY Gained*	Cost per Life Year Gained*	Cost per Additional Year Without a Wheelchair (EDSS <7)*†
Tolebrutinib	Best supportive care	$3,400,000	$2,900,000	$7,000,000	$1,500,000

*Based on placeholder price

†Slight changes to the results have been made in between the report posting and the presentation of these results that will be reflected in the final evidence report

One Way Sensitivity Analyses



*Based on placeholder price
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EDSS: expanded disability status scale; QALY: quality-adjusted life year

Probabilistic Sensitivity Analysis

Drug	Cost-Effective at $50,000 per QALY and evLY*	Cost-Effective at $100,000 per QALY and evLY*	Cost-Effective at $150,000 per QALY and evLY*
Tolebrutinib	0%	0%	0%

*Based on placeholder price

Scenario Analyses (1)

1. Modified societal perspective
2. Alternative stopping rule for tolebrutinib (i.e., once a patient reaches an EDSS score of 7)
3. Inclusion of disability improvement in EDSS health states for the tolebrutinib arm

Treatment	Base-Case Results*	Scenario Analysis 1*	Scenario Analysis 2*†	Scenario Analysis 3*
Tolebrutinib	$3,400,000 per QALY and $2,900,000 per evLY	$3,100,000 per QALY and $2,500,000 per evLY	$3,100,000 per QALY and $2,600,000 per evLY	$1,300,000 per QALY and $1,100,000 per evLY

*Based on a placeholder price

†Slight changes to the results have been made in between the report posting and the presentation of these results that will be reflected in the final evidence report

QALY: quality-adjusted life year; evLY: equal value of life year

Scenario Analyses (2)

4. Using transition probabilities from the London Ontario cohort for the placebo arm

Treatment	Intervention Acquisition Costs*	Intervention-Related Costs†	Non-Intervention Related Costs‡	Total Costs*	QALYs	evLYs	Life Years	Years Without a Wheelchair (EDSS <7)§
Tolebrutinib	$1,565,000	$10,000	$668,000	$2,243,000	4.33	4.66	14.12	5.28
Best Supportive Care	$0	$0	$665,000	$665,000	3.69	3.69	13.60	3.76
Incremental Cost per Outcome					$2,500,000	$1,600,000	$3,000,000	$1,000,000

*Based on placeholder price

†Intervention-related costs include costs of monitoring required for the intervention, as specified in clinical trials, guidelines, or package label

‡Non-intervention related costs include health state costs related and unrelated to SPMS and cost of death

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Health Benefit Price Benchmark (HBPB)

Annual Price Benchmark for Tolebrutinib

Annual Prices Using	Annual Price at $100,000 Threshold	Annual Price at $150,000 Threshold
QALYs Gained	$3,250	$4,900
evLYs Gained	$3,900	$5,900

evLY: equal value life year, QALY: quality-adjusted life year, WAC: wholesale acquisition cost

Limitations

- Primary endpoints do not necessarily reflect transitions between EDSS health states
- Absence of data to inform health state transitions to EDSS 9, which is the most burdensome health state in terms of health state costs and quality of life
- Other data gaps that influenced model decisions include a lack of information on long-term discontinuation, detailed costs across EDSS, and variability in literature-based health-related quality of life values

Comments Received

- Transition probability matrix submitted (in confidence) and updated results from previous draft report.
  - Treatment effects for both progression and improvement applied consistently
- Model structure may not reflect nuanced changes in disability progression.

Conclusions

- Tolebrutinib for the treatment of SPMS is more effective through improving quality of life, length of life, and disability progression compared with best supportive care.
- At the placeholder price of $115,000 per year, tolebrutinib is expected to exceed commonly cited cost-effectiveness thresholds in the US health care system.

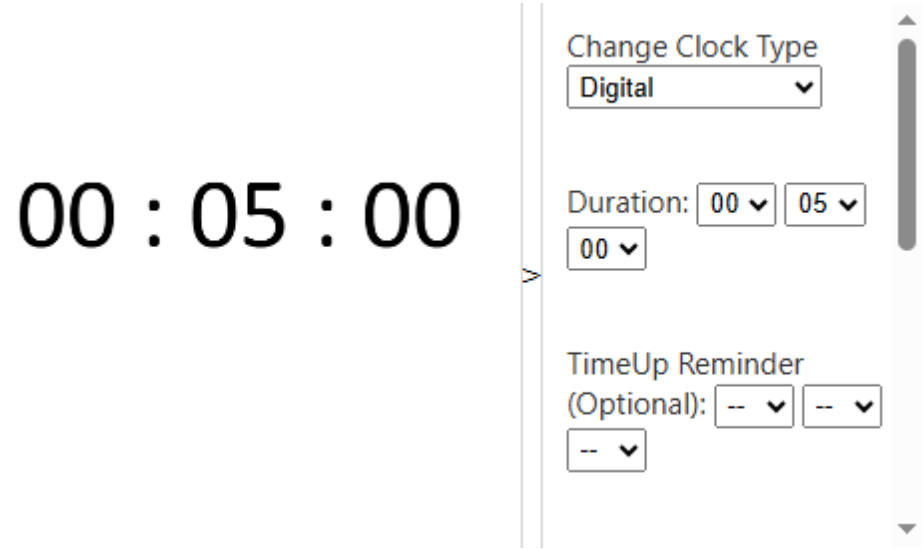
Questions?

Manufacturer Public Comment and Discussion

Luis Felipe Orozco Cabal, MD, PhD
Global Medical Head Neurology, Sanofi

Conflicts of Interest:

- *Dr. Orozco is a full-time employee of Sanofi.*



Lunch

Meeting will resume at 11:50AM PT

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Voting Questions

Patient Population for all questions: *Adults with non-relapsing secondary progressive multiple sclerosis.*

Clinical Evidence

1. **Is the current evidence adequate to demonstrate that the net health benefit of tolebrutinib is greater than that of best supportive care*? *Defined as pharmacological and non-pharmacological treatments to alleviate the symptoms of MS.**

Benefits Beyond Health and Special Ethical Priorities

To help inform judgments of overall long-term value for money, please indicate your level of agreement with the following statements:

2. There is substantial unmet need despite currently available treatments.

3. This condition is of substantial relevance for people from a racial/ethnic group that has not been equitably served by the healthcare system.

To help inform judgments of overall long-term value for money, please indicate your level of agreement with the following statements based on the relative effects of tolebrutinib versus best supportive care:

4. The treatment is likely to produce substantial improvement in caregivers' quality of life and/or ability to pursue their own education, work, and family life.

5. The treatment offers a substantial opportunity to improve access to effective treatment by means of its mechanism of action or method of delivery.

Break

Meeting will resume at 4:00PM ET

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Policy Roundtable

Policy Roundtable

Participant	Conflict of Interest
Robert Bermel, MD, MBA, FAAN, Director, Mellen Center for Multiple Sclerosis, Cleveland Clinic	Dr. Bermel has served as a consultant for Genzyme/Sanofi, Genentech/Roche, Novartis, and TG Therapeutics and received consulting fees in excess of $5,000. He also serves as a volunteer member of the Medical Advisory Board, which has received >25% of its funding from healthcare companies.
Kathleen Costello, CRNP, MSCN, Interim CEO, Consortium of MS Centers; President, Multiple Sclerosis Foundation	The Consortium of MS Centers and Can Do MS receive sponsorships and educational grants from the following Pharmaceutical Companies: Amgen, Biogen, EMD Serono, Bristol Myers Squibb, Genentech, Kyverna, Novartis, Sandoz, Sanofi, Octave Bioscience, TG Therapeutics, Vanda and Viatris. Kathleen Costello has no personal disclosures.
Aaron Dush, PharmD, Senior Clinical Pharmacist, UnitedHealthcare	Dr. Dush is a full-time employee of UnitedHealthcare.
Lisa Farnett, PharmD, Global Medical Director, Sanofi	Dr. Farnett is a full-time employee of Sanofi.
Nancy Garcia, MTS, BCC, Retired Chaplain	No conflicts to disclose.
Ellen Mowry, MD, MCR, Professor of Neurology & Epidemiology, Johns Hopkins University	Johns Hopkins University has received funding from Roche/Genentech and Biogen.
Jeff White, PharmD, MS, Staff Vice President, Clinical Pharmacy Services, Elevance Health	Dr. White is a full-time employee of Elevance Health.

CTAF Council Reflections

Next Steps

- Meeting recording posted to ICER website next week
- Final Report published on or around July 15, 2025
    - Includes description of CTAF votes, deliberation, policy roundtable discussion
- Materials available at: https://icer.org/assessment/multiple-sclerosis-2025/

Adjourn

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