Treatments for Spinal Muscular Atrophy: Effectiveness and Value

Public Meeting — August 1, 2025

Meeting materials available at: https://icer.org/assessment/spinal-muscular-atrophy-2025/

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MIDWEST CEPAC
COMPARATIVE EFFECTIVENESS PUBLIC ADVISORY COUNCIL

Participating Members of the Midwest CEPAC

Jill Johnson, PharmD, BCPS, Midwest CEPAC Chair,
Professor, College of Pharmacy, University of Arkansas for Medical Sciences

- **Bijan Borah, PhD,** Professor of Health Services Research, Mayo Clinic College of Medicine and Science
- **Kurt Vanden Bosch, PharmD,** System Formulary Lead at St. Luke's Health System
- **Donald Casey, MD, MPH, MBA, MACP, FAHA,** Associate Professor of Internal Medicine, Rush Medical College
- **Sneha Dave,** Executive Director, Generation Patient
- **Stacie Dusetzina, PhD,** Professor of Health Policy, Vanderbilt University Medical Center
- **Jayani Jayawardhana, PhD,** Associate Professor, University of Kentucky
- **David Kim, PhD,** Assistant Professor, University of Chicago
- **Bradley C Martin, PharmD, PhD,** Professor, University of Arkansas for Medical Sciences
- **Timothy McBride, PhD,** Professor, Washington University in St. Louis
- **Reem Mustafa, MD, MPH, PhD, FACP,** Professor of Medicine, Division of Nephrology & Hypertension, The University of Kansas Medical Center
- **Rachel Sachs, JD, MPH**, Professor of Law, Washington University in St. Louis School of Law
- **Stuart Winston, DO,** Patient Experience Lead Consultant, Trinity Health IHA Medical Group

Patient Experts

Giles Lomax, CEO, SMA UK

SMA UK received 15.6% of income from pharmaceutical companies including Scholar Rock, Biogen, Novartis and Roche in 2024/2025.

Portia Thorman, Head of Advocacy and Community, SMA UK

SMA UK received 15.6% of income from pharmaceutical companies including Scholar Rock, Biogen, Novartis and Roche in 2024/2025.

Clinical Experts

Thomas Crawford, MD, Professor of Neurology and Pediatrics, Johns Hopkins Hospital

Dr. Crawford has served as consultant on advisory panels to Biogen, Avexis, Scholar Rock, Muscular Dystrophy Association, SMA Foundation and CureSMA. Dr Crawford has received compensation for continued conductance of clinical trials by Biogen, Novartis/Avexis, Sarepta, and Scholar Rock, as well as monetary support for participation in advisory boards by Biogen and Scholar Rock in the last 36 months.

Hugh McMillan, MD, Pediatric Neurologist, Children's Hospital of Eastern Ontario (CHEO)

Dr. McMillan has served as a consultant and principal investigator for clinical trials for Novartis, Roche, and Biogen with funds provided to institution.

ICER Speakers

Sarah K. Emond, MPP
President & CEO

Linda Luu, MSc
Lead Modeler,
Research Scientist, Department of Pharmacy, University of Washington

David Rind, MD, MSc
Chief Medical Officer and Practicing Physician

Jeffrey A. Tice, MD
Evidence Author,
Professor of Medicine, University of California, San Francisco

Why are we here today?

“Every single time I attempt to eat a bowl of soup or reach my canvas while painting a picture, I know I am getting weaker. Everyday wins would be things like improved respiratory function, skills for life improvement, like being able to pull up the blanket to cover yourself in bed, independently use the toilet, to put your own shoes on, and keep up with peers without excessive fatigue.”

Cure SMA’s Voice of the Patient Report for SMA

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**

WHO PAYS FOR RISING HEALTH CARE PRICES?

NBER

National Bureau of Economic Research

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

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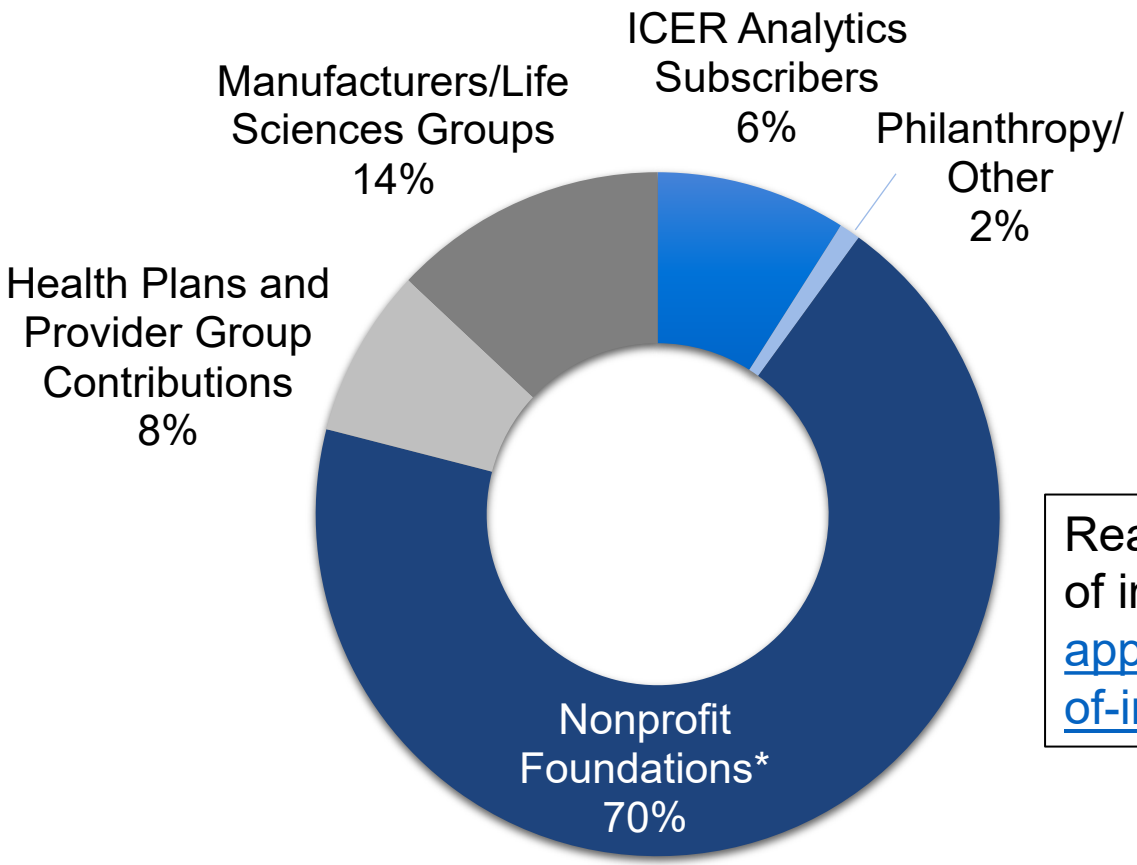
2025 Funding and Managing COIs



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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 Washington**

- **John Brandsema, MD,** Pediatric Neurologist, Children's Hospital of Philadelphia
- **Jenna Klotz, MD, MS,** Clinical Assistant Professor, Stanford University School of Medicine, Stanford Children's Health
- **Praveen Thokala, PhD,** Director, PT Health Economics Ltd, UK
- **Portia Thorman,** Head of Advocacy and Community, Spinal Muscular Atrophy, UK

Structured to support **Midwest CEPAC** voting and policy discussion

Value Assessment Framework: Long-Term Value for Money

Agenda (CT)

10:00 AM	Meeting Convened and Opening Remarks
10:20 AM	Presentation of the Clinical Evidence
11:00 AM	Presentation of the Economic Model
11:40 AM	Public Comments and Discussion
12:00 PM	Lunch Break
12:50 PM	Midwest CEPAC Deliberation and Vote
1:50 PM	Break
2:00 PM	Policy Roundtable Discussion
3:30 PM	Reflections from Midwest CEPAC
4:00 PM	Meeting Adjourned

Presentation of the Clinical Evidence

Jeffrey A. Tice, MD

Professor of Medicine

University of California, San Francisco

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Therapies for the Treatment of Spinal Muscular Atrophy
Team Introductions

Team Member	Title
Jeffrey A. Tice, MD	**Evidence Author and Professor of Medicine, UCSF**
Dmitriy Nikitin, MSPH	**Senior Research Lead, ICER**
Sol Sanchez, BA	**Research Assistant, ICER**

Disclosures

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

JT has no conflicts to disclose.

DN and SS are employees of ICER and have no conflicts to disclose.

ICER's full policy for managing and disclosing potential conflicts of interest can be found here.

Spinal Muscular Atrophy (SMA)

Disease Background

- Genetic deficiency of SMN1 protein
- Progressive loss of motor neurons
- Progressive muscle weakness
  - Unable to breathe
  - Unable to swallow
  - Unable to crawl, sit, or stand

SMN1: survival motor neuron 1

SMA Clinical Classification

SMA Type	SMN2 Copy Number*	Age of Symptom Onset	Highest Achieved Motor Function	Natural Age of Death
0	0-1	Prenatal/ Fetal	None	<6 months
1	1-3	<6 months	Sit with support only	<2 years
2	2-4	6–18 months	Sit independently	>2 years
3	3-4	>18 months	Walk independently	Adulthood
4	4 – 8	Adult (2nd or 3rd decade)	Walk during adulthood	Adult

SMA: spinal muscular atrophy, SMN2: survival motor neuron 2

Impact on Patients

- It used to be a fatal disease
- Disease-modifying therapy's impact on respiratory function is lifesaving
- Intrathecal therapy can be traumatic for young patients and can require general anesthesia
- Among adults, gaining muscle strength is their greatest unmet need
- Fatigue is an important issue for older patients and has not been well studied
- Financial toxicity is a major issue for patients and their caregivers

Standard of Care and Management

- Nusinersen (Spinraza®) is an antisense oligonucleotide that targets *SMN2* so that it creates more functional SMN protein. It is administered via intrathecal injection every four months after the loading dose.
- Onasemnogene abeparvovec (Zolgensma®) is a gene therapy that delivers a functional copy of the *SMN1* gene as a one-time intravenous (IV) infusion.
- Risdiplam (Evrysdi®) is a splicing modifier that targets *SMN2* to increase the production of SMN. It is an oral medication taken once daily.

SMN: survival motor neuron

Scope of Review

- Q1: What is the comparative clinical effectiveness and economic value of apitegromab as an add-on therapy to background disease-modifying therapy (nusinersen or risdiplam)?
- Q2: What is the net health benefit of risdiplam or nusinersen as add-on therapy in patients previously treated with onasemnogene abeparvovec?
- Q3: Is there a comparative advantage for first-line therapy in asymptomatic infants between nusinersen, onasemnogene abeparvovec, and risdiplam?

Apitegromab

- Selective inhibitor of a myostatin precursor
- Myostatin inhibits muscle growth and strength; inhibiting myostatin may increase muscle size and strength
- Given by IV infusion every four weeks

IV: intravenous

Outcomes

- Hammersmith Functional Motor Scale – Expanded (HFMSE)
  - 33-item scale with maximum score of 66
  - MCID 3-point change, though some controversy
- Motor milestones
  - Sitting without support, standing with assistance, walking alone…
- Quality of life, mental health, swallowing, fatigue, muscle strength

MCID: minimum clinically important difference

Clinical Evidence

Q1: Evidence Base for Apitegromab Added to SMN-directed therapy

Trials	Description
SAPPHIRE, unpublished	• Phase III RCT: 10 mg/kg and 20 mg/kg versus placebo • Patients aged 2-12 years with Type 2 or 3 SMA • Receiving either nusinersen or risdiplam
TOPAZ	Phase II: Dose finding study (2 or 20 mg/kg)
ONYX	Long-term, open-label extension of SAPPHIRE and TOPAZ

mg/kg: milligrams per kilograms, QALY: quality-adjusted life years, RCT: randomized controlled trial, SMA: spinal muscular atrophy, SMN: survival motor neuron

Pooled SAPPHIRE Trial Results at One Year

	Apitegromab	Placebo	Difference	P-value
HFMSE change from baseline	+0.6	-1.2	1.8 (0.3 to 3.3)	0.02
≥3-point improvement	30.4%	12.5%	17.9%	0.03
≥0-point improvement	62.7%	50.0%	12.7%	NR

HFMSE: Hammersmith Functional Motor Scale – Expanded, NR: not reported

TOPAZ: Stable HFMSE for four years in 23 patients receiving apitegromab

Harms

	Apitegromab	Placebo
SAE	19.8%	10%
- Pneumonia	6.6%	0%
- Dehydration	2.8%	0%
Discontinuation due to AE	0%	0%

AE: adverse events, SAE: serious adverse events

Controversies and Uncertainties

Key Points

- **Dose for apitegromab**: 10 mg/kg group had nominally greater improvement in HFMSE than the 20 mg/kg group
- No data in patients with Type 1 or 4 SMA
- No data in patients who have received gene therapy

HFMSE: Hammersmith Functional Motor Scale – Expanded, mg/kg: milligrams per kilograms, SMA: spinal muscular atrophy

Benefits Beyond Health and Special Ethical Priorities

Key Points

- Current therapies slow the decline, but do not restore lost function. There is a **substantial unmet need** to improve strength, function, and reduce fatigue.
- The net health benefits of apitegromab are at best small, though this may have some **impact on caregiver quality of life** as modeled in the modified societal perspective.
- Apitegromab requires an IV infusion every four weeks, which requires travel to an infusion center or coordination with a home infusion program, which will be a **burden** for many patients and their caregivers.

IV: intravenous

Public Comments Received

- HFMSE MCID of 3 is outdated
  - Scholar Rock did not provide additional data as requested
  - Data on disease stability (change ≥0 points) added
- Observed incidence of pneumonia is in line with that observed in other clinical trials

HFMSE: Hammersmith Functional Motor Scale – Expanded,
MCID: minimum clinically important difference

Summary

- Small improvement in function 0.6 versus -1.2 on 66-point scale
- Phase II study suggests stability of HFSME gains for four years
- Signal of harms: 20% SAEs versus 10%
- Primary data from one unpublished study of 156 patients with one year follow up

HFMSE: Hammersmith Functional Motor Scale – Expanded,
SAEs: serious adverse events

ICER Evidence Ratings for Apitegromab

Treatment	Comparator	Population	Evidence Rating
Apitegromab	Best Supportive Care	Patients ages 2-12 years with Type 2 or 3 SMA receiving treatment with nusinersen or risdiplam	P/I: Promising, but inconclusive

SMA: spinal muscular atrophy

Q2: SMN-Targeted Therapy After Gene Therapy

- **Nusinersen**
  - RESPOND study: Uncontrolled study of nusinersen in patients with 2 copies of *SMN2* followed for 302 days
    - Cohort 1: 21 patients with nusinersen ≤9 months of age.
      - Increase of 8.7 points on the HINE-2
    - Cohort 2: 13 patients with nusinersen >9 months of age.
      - Increase of 6.9 points on the HINE-2
    - Study completion October 2025 with 778 days of follow-up

HINE-2: Hammersmith Infant Neurological Exam Section 2, SMN2: survival motor neuron 2

Q2: SMN-Targeted Therapy After Gene Therapy

- **Risdiplam**
  - JEWELFISH: 14 patients with 1 to 3 copies of *SMN2*
    - At 104 weeks, 9/14 patients had an increase of ~7 points on the HFMSE
    - Two Phase IV studies initiated in this population
  - US Multicenter study: 20 patients with 2 or 3 copies of *SMN2*
    - Some patients had improvements in swallowing
    - Some patients had improvements in respiratory function
    - 9/9 patients assessed with HFMSE saw stability or improvement

HFMSE: Hammersmith Functional Motor Scale Expanded, *SMN2*: survival motor neuron 2

Harms of SMN-Targeted Therapy After Gene Therapy

- Nusinersen
  - Complications of LP (headache, back pain, vomiting)
- Risdiplam
  - More fever, diarrhea, rashes, arthralgias than control patients

LP: lumbar puncture, SMN: survival motor neuron

Controversies and Uncertainties

- Studies are small and uncontrolled
- As young children grow, they reach new developmental milestones: treatment or natural history?

ICER Evidence Ratings for SMN directed therapy after gene therapy

Treatment	Comparator	Population	Evidence Rating
Nusinersen	Best Supportive Care	Patients with type 1 or 2 SMA previously treated with gene therapy	P/I: Promising, but inconclusive
Risdiplam	Best Supportive Care	Patients with type 1 or 2 SMA previously treated with gene therapy	C++: Comparable or better

SMA: spinal muscular atrophy, SMN: survival motor neuron

Q3: First line therapy in asymptomatic infants

- No head-to-head trials of nusinersen, onasemnogene abeparvovec, or risdiplam.
- All three have strong evidence of benefit regarding survival, avoidance of permanent ventilation, achievement of motor milestones compared with historical data.
- Differences in study populations and design preclude NMA.

NMA: network meta-analysis

ICER Evidence Ratings for First Line Therapy

Treatment	Comparator	Population	Evidence Rating
Risdiplam	Nusinersen	Untreated patients with any type of SMA at any age	I: Insufficient
Risdiplam	Onasemnogene abeparvovec	Untreated patients with any type of SMA at any age	I: Insufficient
Nusinersen	Onasemnogene abeparvovec	Untreated patients with any type of SMA at any age	I: Insufficient

SMA: spinal muscular atrophy

Questions?

Presentation of the Economic Model

Linda Luu, MSc

Research Scientist

Department of Pharmacy, University of Washington

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Therapies for the Treatment of Spinal Muscular Atrophy
Team Introductions

Team Member	Title
Linda Luu, MSc	Lead Modeler and Research Scientist, University of Washington
Josh Carlson, PhD	Professor & Graduate Program Director, Choice Institute, University of Washington
Woojung Lee, PharmD, PhD	Associate Director of Health Economics and Decision Modeling, ICER
Marie Phillips, BA	Health Economics Research Assistant, ICER
Hui-Hsuan Chan, MHS	PhD Student, University of Washington

Disclosures

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

WL and MP are employees of ICER and have no conflicts to disclose.

JC has received consulting fees from Genentech, not related to SMA.

The other members of the University of Washington Modeling team (LL and HC) have no relevant conflicts to disclose.

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Objective

To evaluate the lifetime cost-effectiveness of apitegromab + standard of care (SoC) treatments nusinersen/risdiplam compared to SoC alone for the treatment of non-ambulatory Type 2/3 SMA in patients aged 2-12.

SMA: spinal muscular atrophy

Unmet Need

Condition	Absolute evLY Shortfall	Proportional evLY Shortfall
Type 2/3 SMA	58.2	94.7%
Other Example Conditions		
Pediatric B-Cell Acute Lymphoblastic Leukemia	53.9	93.9%
Multiple Sclerosis	18.9	52%
Osteoporosis	2.6	19%

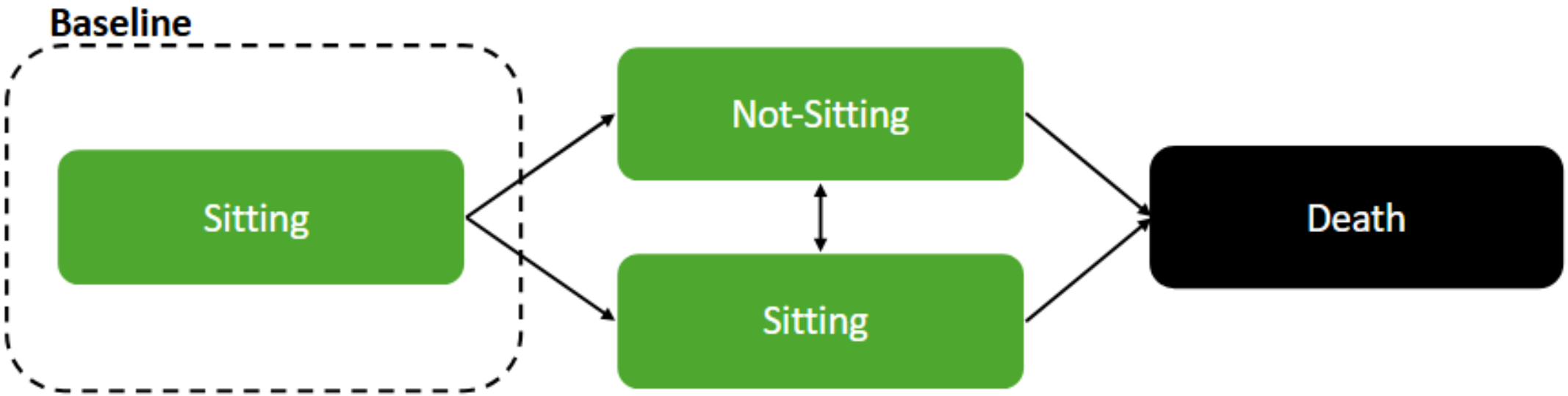
evLY: equal value life years, SMA: spinal muscular atrophy

Methods in Brief

Methods Overview

Domain	Approach
Model	Markov Model
Setting	United States
Perspective	Health Care System Perspective and Modified Societal 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; equal value of life years (evLY) gained

Model Schematic



"Sitting" represents an aggregate of multiple granular health states (e.g., sitting with assistance, sitting independently).

Model Cohort Characteristics

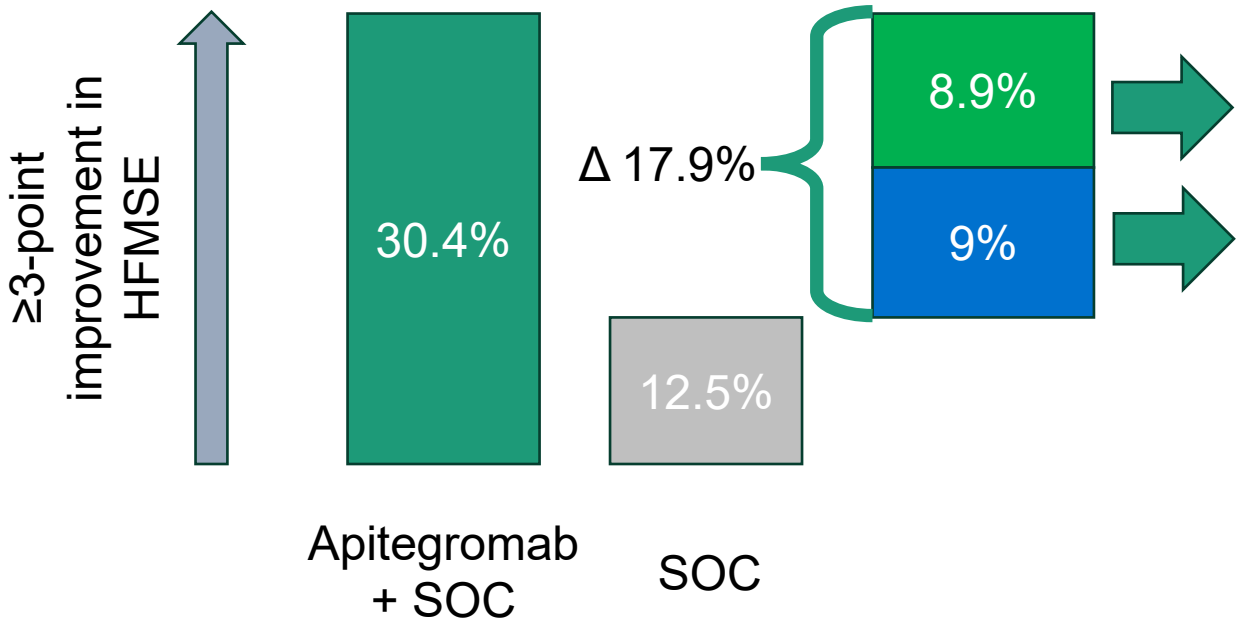
Baseline Characteristic	Value	Source
Mean Age in Years (Range)	7.8 (2, 12)	SAPPHIRE trial: Pooled data from participants aged 2-12 years
Percent Female (%)	47.4	
Nusinersen/Risdiplam (%)	77.6/22.4	
Mean Duration of Nusinersen/Risdiplam (Years)	5.0/3.0	
SMA Type 2/3 (%)	89.1/10.9	
Mean Baseline HFMSE Score (Range)	26.2 (9, 48)	

HFMSE: Hammersmith Functional Motor Scale – Expanded, SMA: spinal muscular atrophy

Key Assumptions

- Patients begin in the “sitting” health state
- No transitions to new mobility states above “sitting”
- Treatment effects achieved at the end of SAPPHIRE are maintained throughout the lifetime
- Disease progression follows a constant rate of HFMSE score decline
- Patients receiving apitegromab begin progressing after four years
- No discontinuation for any of the treatments

Treatment-Related Efficacy & Health State Utilities



+ 0.06 utility gain: Patients with ≥3 pt. increase in HFMSE, without WHO milestone improvement

+ 0.08 utility gain: Patients with ≥3 pt. increase in HFMSE, with WHO milestone improvement

- Remaining apitegromab patients stay at mean health state specific utility
- 3% of SOC patients have a utility decrement (-0.02) due to WHO milestone worsening, remaining 97% stay at mean health state specific utility

HFMSE: Hammersmith Functional Motor Scale – Expanded, SoC: standard of care, pt: point, WHO: World Health Organization

Treatment-Related Efficacy & Health State Utilities

Utility increments were applied to baseline utilities from Belter et al. 2020 that used Health Utilities Index Mark 3 (HUI3) values from 2019 Cure SMA Community Update Survey Data

Health State	Utility		Source
	Apitegromab + SoC	SoC	
Sitting	0.27	0.26	Belter et al. 2020 Incremental utilities from Lloyd et al. 2019 & Hu et al. 2022
Not-Sitting	0.14	0.12	

SoC: Standard of Care

Treatment-Related Efficacy & Health State Utilities (Modified Societal Perspective)

We incorporated caregiver utilities through an additive approach:

1 caregiver + 1 patient = 1 family QALY/evLY

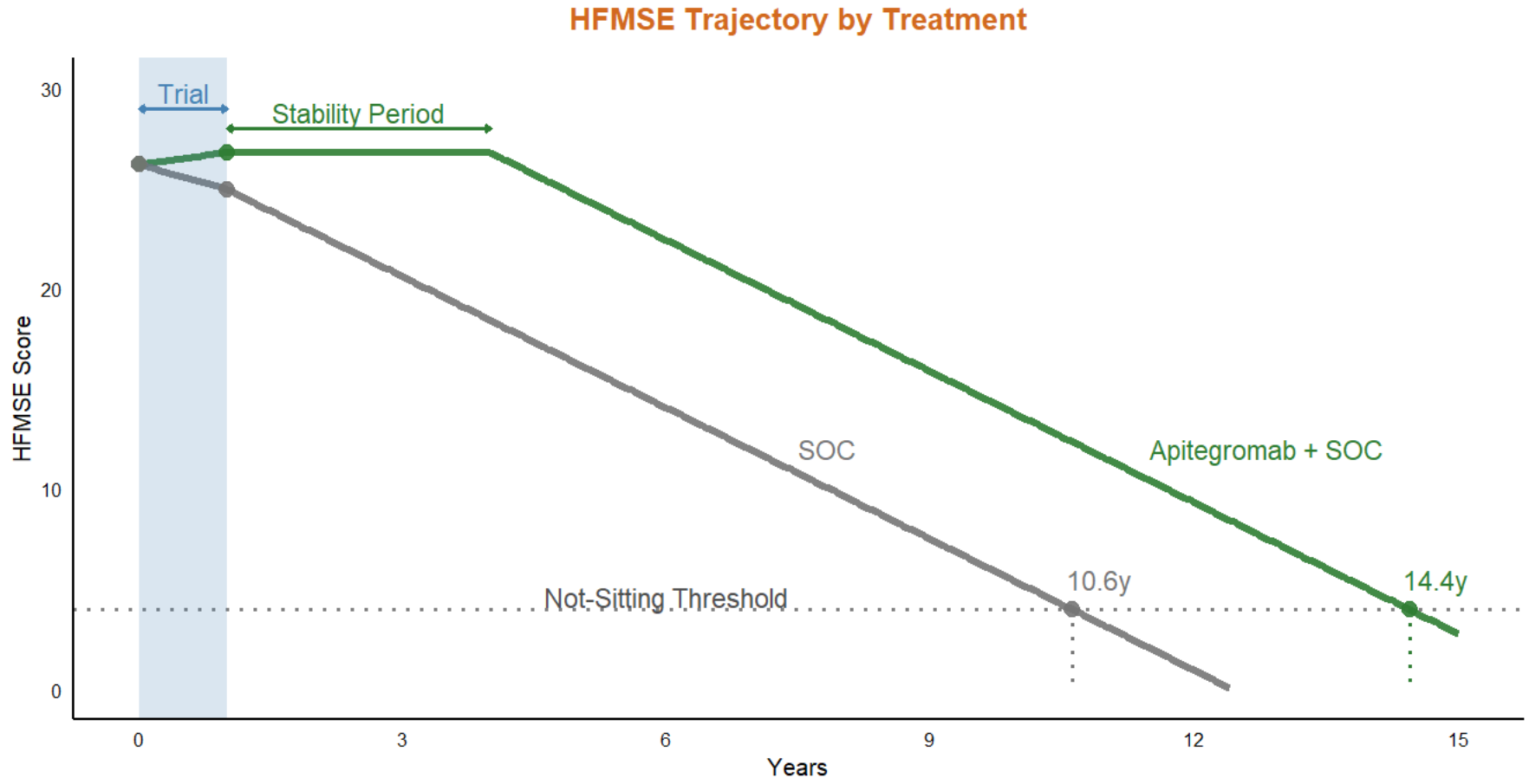
- Caregiver utilities were derived from López-Bastida et al. 2017, Spanish subgroup (via NICE Technology Appraisal for nusinersen).
- Bereavement disutilities were obtained from Tara Lavelle (unpublished) applied for 20 years post patient death. These disutilities varied by time since death (<5 years, 5-10 years, 10-20 years) and were originally derived from Type 1 patients, introducing some uncertainty.

Health State	Caregiver Utility	Source
Sitting	0.592	López-Bastida et al. 2017
Not-Sitting	0.484	

QALY: quality adjusted life year, evLY: equal value of life year

Disease Progression

- Assumed parallel HFMSE decline in both treatments based on clinical expert opinion
- Obtained HFMSE decline rate from SAPPHIRE placebo arm



HFMSE: Hammersmith Functional Motor Scale Expanded, SoC: standard of care

Mortality & Serious Adverse Events

- Mortality followed previous approach from the ICER 2019 model, using a separate mortality model for each health state
- Pneumonia was classified as a serious adverse event and incorporated into the economic model with an assumed duration of one month
- A scenario analysis excluding pneumonia was conducted to test model sensitivity

Treatment Costs

Intervention (Dosage)	Annual WAC/Placeholder Price	Net Annual Cost	Source
Apitegromab	$350,000*	$350,000*	IPD Analytics
Nusinersen (12 mg/4 months)	$448,916†	$448,916†	CMS APC
Risdiplam (5 mg/daily)	$409,446	$358,265	REDBOOK 12.5% discount from IPD Analytics

APC: Ambulatory Payment Classifications, CMS: Centers for Medicare & Medicaid Services, mg: milligrams, WAC: Wholesale Acquisition Cost
*Placeholder price
†Calculated from APC cost from CMS - includes a 6% markup

Results

Base-Case Results – Health Care System Perspective

Treatment	Total Costs	QALYs	evLYs	Life Years
Apitegromab* + SoC	$11,038,000	3.38	4.66	13.89
SoC	$5,324,000	2.64	2.64	11.95
Incremental†	$5,714,000	0.74	2.02	1.94

Treatment	Comparator	Cost per QALY Gained	Cost per evLY Gained
Apitegromab* + SoC	**SoC**	$7,702,000	$2,829,000

evLYs: equal value of life years, QALYs: quality-adjusted life years, SoC: standard of care
*Based on placeholder price of $350,000 per year
†Any discrepancies in incremental results are due to rounding

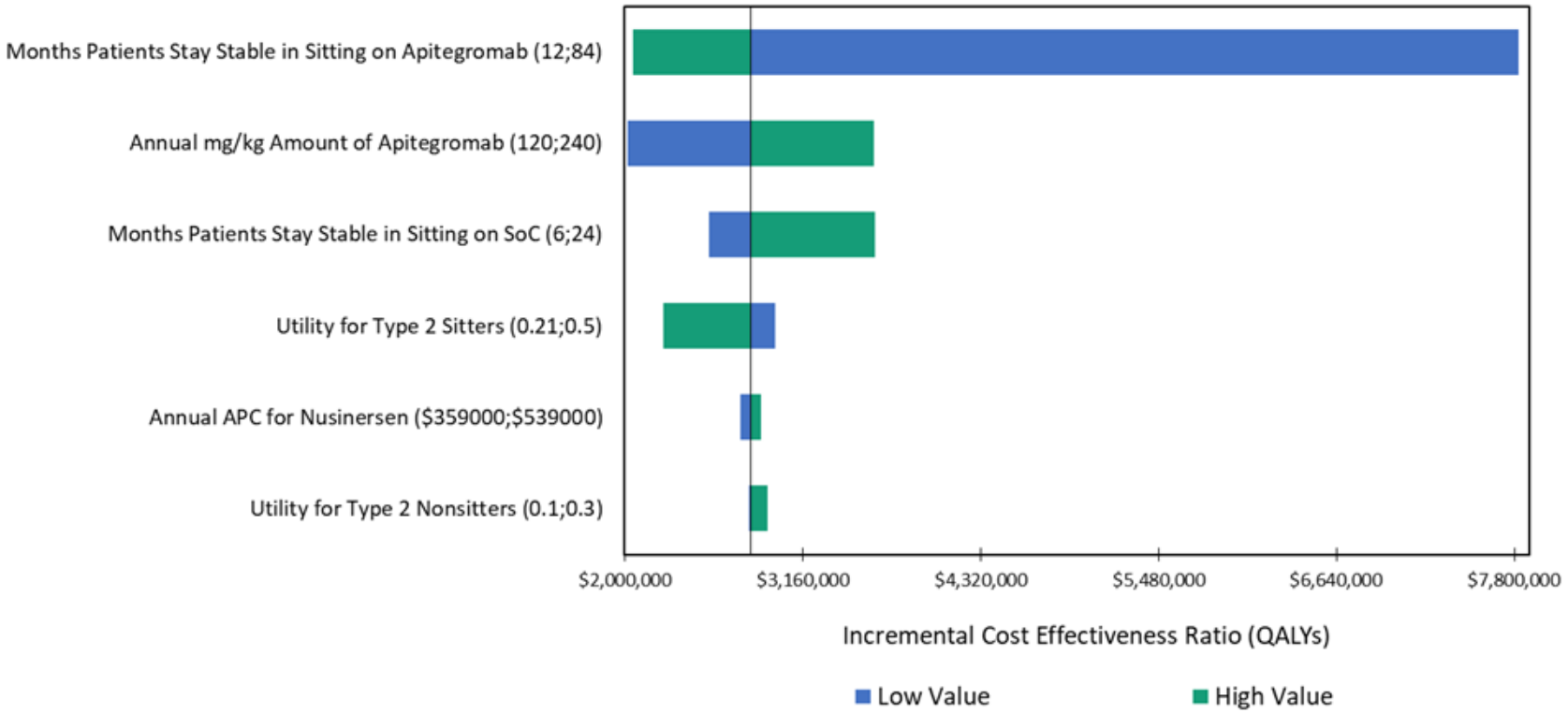
Base-Case Results – Modified Societal Perspective

Treatment	Total Costs	QALYs	evLYs	Life Years
Apitegromab* + SoC	$11,038,000	10.46	11.73	13.89
SoC	$5,324,000	8.43	8.43	11.95
Incremental†	$5,714,000	2.02	3.30	1.94

Treatment	Comparator	Cost per QALY Gained	Cost per evLY Gained
Apitegromab* + SoC	**SoC**	$2,823,000	$1,730,000

evLYs: equal value of life years, QALYs: quality-adjusted life years, SoC: standard of care
*Based on placeholder price of $350,000 per year
†Any discrepancies in incremental results are due to rounding

One Way Sensitivity Analyses – Modified Societal Perspective



Based on placeholder price of $350,000 per year

In both base cases, apitegromab + SoC was not cost-effective at any of the common price thresholds ($50,000, $100,000, $150,000, $200,000 per QALY or evLY gained) across 1000 PSA simulations.

SoC: standard of care, HFMSE: Hammersmith Functional Motor Scale Expanded, PSA: probabilistic sensitivity analysis, WHO: World Health Organization

Scenario Analyses

Scenario	Health Care System Perspective		Modified Societal Perspective	
	Cost per QALY Gained	Cost per evLY Gained	Cost per QALY Gained	Cost per evLY Gained
Base Case	$7,702,000	$2,829,000	$2,823,000	$1,730,000
ICER Reference Case: Removal of Costs	$6,567,000	$2,412,000	$2,407,000	$1,475,000
Exclusion of Pneumonia	$7,695,000	$2,828,000	$2,822,000	$1,730,000
No Disease Progression on Apitegromab	$3,925,000	$1,483,000	$1,337,000	$856,000

Based on placeholder price of $350,000 per year

QALY: quality adjusted life year, evLY: equal value of life years, WHO: World Health Organization

Health Benefit Price Benchmark (HBPB)– ICER Reference Case

Annual Prices Using…	Annual WAC*	Annual Price at $100,000 Threshold	Annual Price at $150,000 Threshold	Discount from WAC* to Reach Threshold Prices
Health Care System Perspective				
QALYs Gained	$350,000*	$4,600	$7,300	(97.91%-98.69%)
evLYs Gained		$13,800	$21,100	(93.97%-96.06%)
Modified Societal Perspective				
QALYs Gained	$350,000*	$10,700	$16,400	(95.31%-96.94%)
evLYs Gained		$19,900	$30,200	(91.37%-94.31%)

*Based on placeholder price of $350,000 per year
WAC: wholesale acquisition cost, QALYs: quality adjusted life years, evLYs: equal value of life years

Limitations

Top Limitations

- Limited data on treatment effect
  - Only unpublished 12-month SAPPHIRE data available
- Utility values
  - Most based on functional classifications (ex. WHO milestones), rather than by HFMSE score changes
- Disease progression uncertainty
- Modeled life extension however there is currently no evidence of life extension

HFMSE: Hammersmith Functional Motor Scale Expanded,
WHO: World Health Organization

Comments Received

- **Oversimplified model structure:** Stakeholders argued the state-transition framework fails to capture small but meaningful motor improvements and the multifaceted impact of SMA beyond motor function that patients and families highly value
- **SMA results in progressive nerve degeneration**, leading to loss of motor function and diminished independence even with current SoC treatments
- Model assumes **disproportionate harms from pneumonia**
- Model uses **outdated and unsupported clinical thresholds** of ≥3-points increase in HFMSE

HFMSE: Hammersmith Functional Motor Scale Expanded, SMA: spinal muscular atrophy, SoC: standard of care

Conclusions

- Apitegromab + SoC provided modest gains in QALYs and evLYs but exceeds standard cost-effectiveness thresholds at the placeholder price of $350,000 annually
- Substantial price reductions exceeding 90% from the placeholder price is required *even after* excluding all costs aside from apitegromab administration costs in both the health-care system and modified societal perspectives
- Results have substantial uncertainty given limited long-term data and inherent challenges modeling rare disease progression
- Our model provides initial cost-effectiveness estimates can be updated as additional evidence becomes available

evLY: equal value life years, QALY: quality adjusted life years, SoC: standard of care

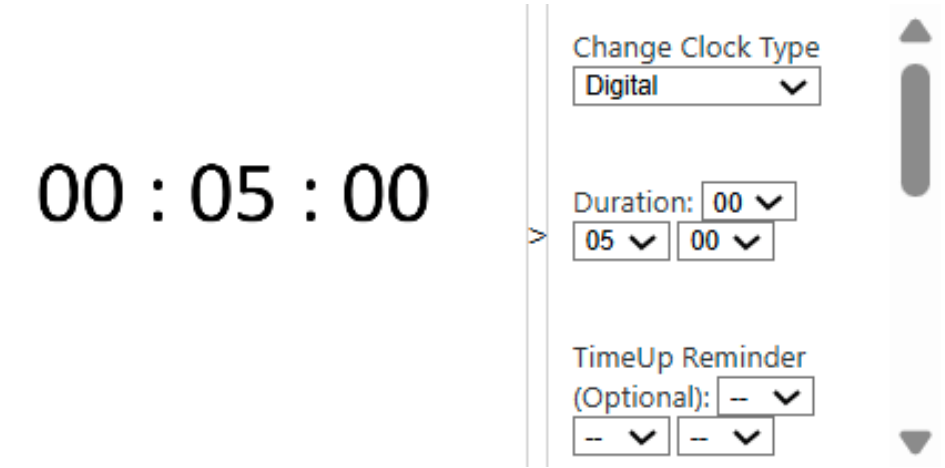
Questions?

Manufacturer Public Comment and Discussion

Thomas Brown, PhD, Vice President, Global Medical Affairs, Scholar Rock

Conflicts of Interest:

- *Dr. Brown is a full-time employee of Scholar Rock.*
- *Dr. Brown has collaborated with SP Consulting, LLC and Value Matters, LLC to compose this public comment.*

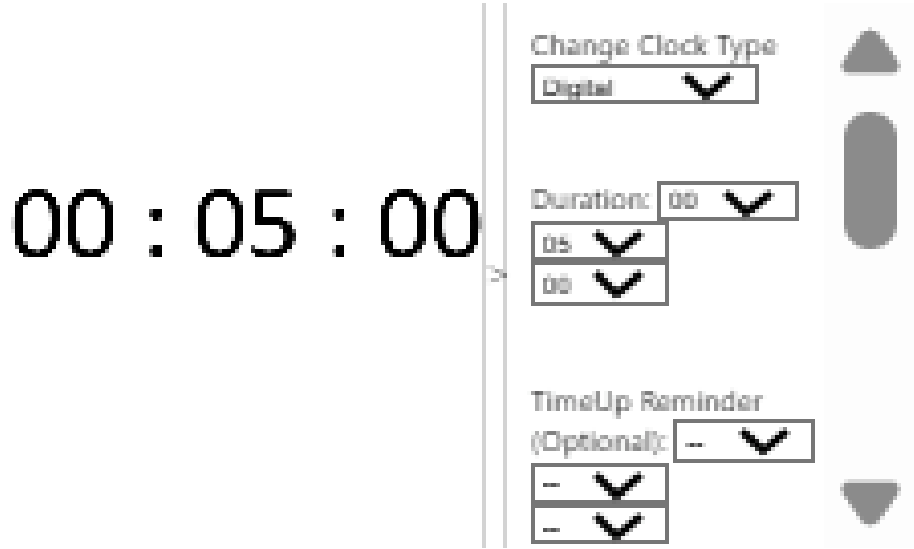


Public Comment and Discussion

Susi Vander Wyk, Executive Director
CureSMA Canada

Conflicts of Interest:

- *Susi is a full-time employee of CureSMA Canada*



Lunch

Meeting will resume at 12:50PM CT

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Voting Questions

Clinical Evidence

Population: For children aged 2-12 years with SMA Type 2 or 3.

1. Is the currently available evidence adequate to demonstrate that the net health benefit of apitegromab in addition to standard of care (risdiplam or nusinersen) is greater than that of standard of care alone?

Population: For people with SMA previously treated with onasemnogene abeparvovec.

2. Is the currently available evidence adequate to demonstrate that the net health benefit of risdiplam is greater than that of no additional treatment?

Population: For people with SMA previously treated with onasemnogene abeparvovec.

3. Is the currently available evidence adequate to demonstrate that the net health benefit of nusinersen is greater than that of no additional treatment?

Population: For clinically presymptomatic infants with SMA.

4. Is the currently available evidence adequate to distinguish the net health benefit among nusinersen, onasemenogene abeparvovec and risdiplam as first line therapy?

4a. If yes, which is best?

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:

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

6. This condition is of substantial relevance for people from a racial/ethnic group that have 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 apitegromab in addition to standard of care (risdiplam or nusinersen) versus standard of care alone:

7. 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.

8. 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 2:00PM CT

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Policy Roundtable

Policy Roundtable

Participant	Conflict of Interest
Thomas Crawford, MD, Professor of Neurology and Pediatrics, Johns Hopkins Hospital	Dr Crawford has received compensation for continued conductance of clinical trials by Biogen, Novartis/Avexis, Sarepta, and Scholar Rock, as well as monetary support for participation in advisory boards by Biogen and Scholar Rock in the last 36 months.
Giles Lomax, CEO, SMA UK	SMA UK received 15.6% of income from pharmaceutical companies including Scholar Rock, Biogen, Novartis and Roche in 2024/2025.
Hugh McMillan, Professor of Pediatrics/Pediatric Neurologist, University of Ottawa/Children's Hospital of Eastern Ontario	Dr. McMillan has served as a consultant and principal investigator for clinical trials for Novartis, Roche, and Biogen with funds provided to institution.
Lindsey Samera, PharmD, Manager Outcomes Based Contracting & Pharmacy Programs, United Healthcare	Dr. Samera is a full-time employee of United Healthcare.
Portia Thorman, Head of Advocacy and Community, SMA UK	SMA UK received 15.6% of income from pharmaceutical companies including Scholar Rock, Biogen, Novartis and Roche in 2024/2025.
Emily Tsiao, PharmD, BCPS, Medical Policies Clinical Pharmacist, 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 2, 2025
- Includes description of Midwest CEPAC votes, deliberation, policy roundtable discussion
- Materials available at: https://icer.org/assessment/spinal-muscular-atrophy-2025/

Adjourn

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