Atidarsagene Autotemcel for Metachromatic Leukodystrophy: Effectiveness and Value

Public Meeting — September 29, 2023

Meeting materials available at: https://icer.org/assessment/metachromatic-leukodystrophy-2023/#timeline

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INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

AN ICER PROGRAM
CTAF
CALIFORNIA TECHNOLOGY ASSESSMENT FORUM

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Patient Experts

Maria Kefalas, Ph.D., Founder, Cure MLD; Professor, Saint Joseph's University

- *Cure MLD has received grants from Bluebird Bio, Homology Medicines, Orchard Therapeutics, Takeda Pharmaceuticals, and Passage Bio, Inc.*

Teryn Suhr, R.N., Executive Director, MLD Foundation

- *MLD Foundation has received sponsorships from various biopharma companies for their annual family conference.*
- *Mrs. Suhr has equity interests such as individual stocks, stock options, or other ownership interests in excess of $10,000 in Orchard Therapeutics.*

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Clinical Experts

Francesca Fumagalli, M.D., Ph.D. Neurologist, Pediatric Immunohematology Unit and Department of Neurology, IRCCS San Raffaele Hospital, Milan

- *Dr. Fumagalli is a sub investigator of clinical trials NCT01560182 and NCT03392987 and PI of clinical trial NCT04283227 using OTL-200 sponsored by Orchard Therapeutics. Dr. Fumagalli has received less than $5,000 in honoraria from Orchard Therapeutics and Takeda.*

Paul Orchard, M.D., Director of the Inherited Metabolic and Storage Disease Program, Professor of Pediatric Blood and Marrow Transplantation and Cellular Therapy, University of Minnesota

- *Dr. Orchard's team offers expanded access to OLT-200 in association with Orchard Therapeutics for specific patients. Dr. Orchard has received less than $5,000 in honoraria or consultancies from Orchard Therapeutics.*

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Why are we here today?

Our son’s condition has impacted him immensely as he was once a healthy active child who would always be outside with our dogs or riding his bike, now he is non-mobile, non-verbal, unable to swallow safely so [is] tube fed, he has no voluntary movements of his limbs, and he is starting to lose his sight. He does have a little head control but only for a few seconds before [his] head drops forward.

Parent of child with MLD

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?

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The Impact on Rising Health Care Costs for Everyone

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

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Organizational Overview

- California Technology Assessment Forum (CTAF)
- Institute for Clinical and Economic Review (ICER)

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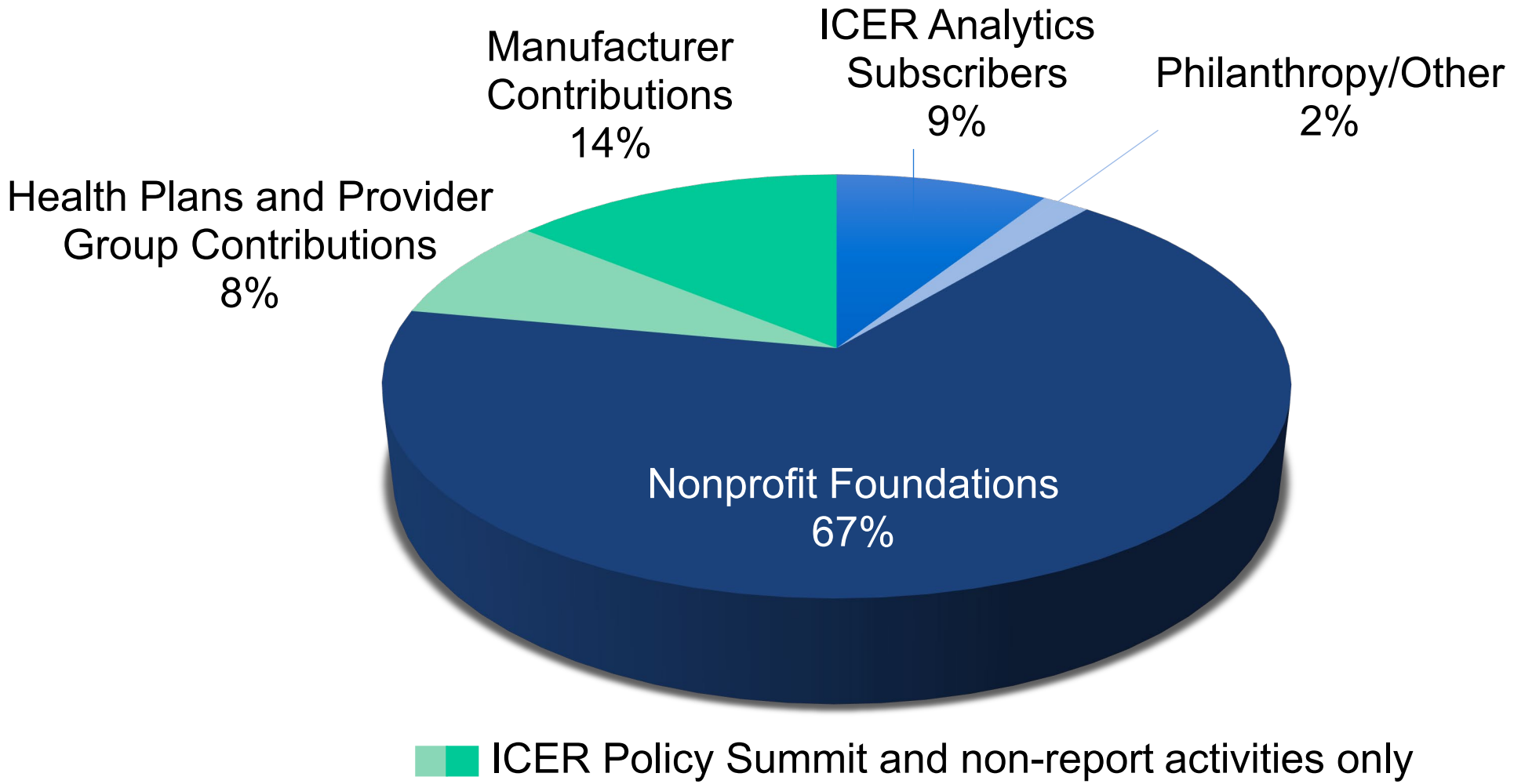
Funding 2023



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How Was the ICER Report Developed?

- Scoping with guidance from patients, clinical experts, manufacturers, and other stakeholders
- Internal ICER evidence analysis and cost-effectiveness modeling
- Public comment and revision
- Expert reviewers
  - **Francesca Fumagalli, M.D., Ph.D.,** Neurologist, IRCCS San Raffaele Hospital, Milan
  - **Paul Orchard, M.D.,** Professor of Pediatrics, University of Minnesota
  - **Teryn Suhr, R.N. and Dean Suhr, B.S.,** Executive Director and President, MLD Foundation
  - **Paul Tappenden, B.A., MSc, Ph.D.,** Professor of Health Economic Modelling, University of Sheffield
- How is the evidence report structured to support CTAF voting and policy discussion?

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Value Assessment Framework: Long-Term Value for Money

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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
11:05 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

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Presentation of the Clinical Evidence

Grace Lin, M.D.

Medical Director for Health Technology Assessment, ICER

Professor of Medicine and Health Policy, UCSF

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Key Collaborators

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- **Finn Raymond, B.S.**, Research Assistant, ICER

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No conflicts to disclose defined as more than $10,000 in health care company stock or more than $5,000 in honoraria or consultancies relevant to this report during the previous year from health care technology manufacturers or insurers.

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Metachromatic Leukodystrophy (MLD)
Overview

- Rare genetic disease, inherited in autosomal recessive fashion

- Affects 1 in 40,000 – 1 in 160,000; about 2,500 people in the US
  - More common in US western Navajo, Alaska Native, and Habbanite Jew populations

- Caused mainly by mutations in the *ARSA* gene, which codes for arylsulfatase A enzyme

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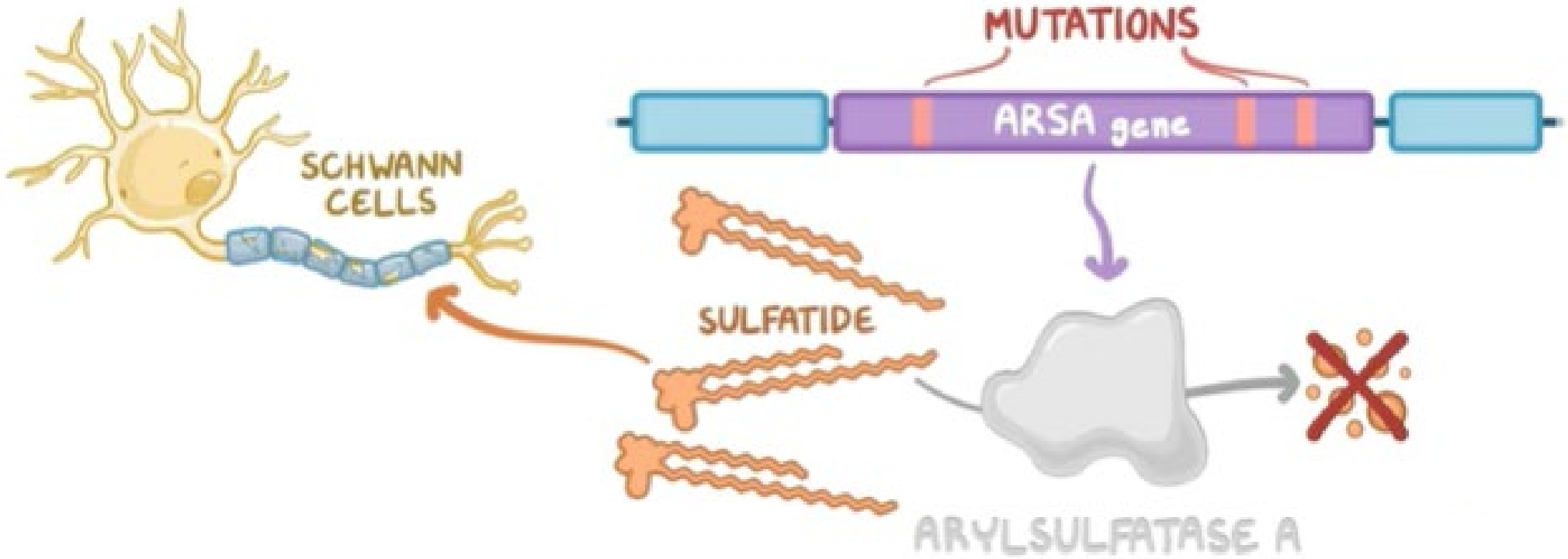
https://mldfoundation.org/mld-101-what.php

Metachromatic Leukodystrophy

What Causes MLD?



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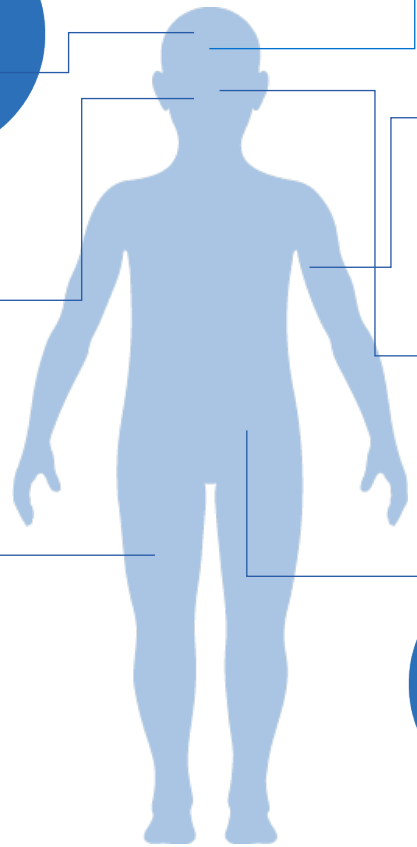
ARSA: arylsulfatase A, MLD: metachromatic leukodystrophy
https://www.youtube.com/watch?v=tSos-AQLwT4&ab_channel=OsmosisfromElsevier

Metachromatic Leukodystrophy

Presentation and Symptoms



Loss of Cognitive Skills

Intellectual, thinking, memory skills

Loss of Motor Skills

Walking, moving, speaking, swallowing

Muscle Weakness

Poor muscle control (ataxia), stiffness, paralysis

Blindness

Progressive loss of vision

Sensation loss

Touch, pain, heat, sound

Emotional/Behavior Problems

Loss of Bladder & Bowel Function

Gallbladder problems

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Metachromatic Leukodystrophy

Classification of Subtypes

Form	Age of Onset	Implications	Population Size
Late Infantile	6-30 months	• Most common form • Presents with difficulty walking, developmental delays • 5–6-year survival after symptom onset	**~50-60%** of patients
Early Juvenile	30 months-7 years	• Slower progression than late infantile, normal development before age 2.5 years • Can present with impaired school performance, cognitive and physical decline • 10–20-year survival estimate after symptom onset	**~20-35%** of patients
Late Juvenile	7-16 years		
Adult	Ages 16+ years	• Slowest progression, normal development before 16 • Psychiatric disorders, progressive dementia • 20–30-year survival estimate after symptom onset	**~15-20%** of patients

Wang et al. ACMG Standards and Guidelines. 2011

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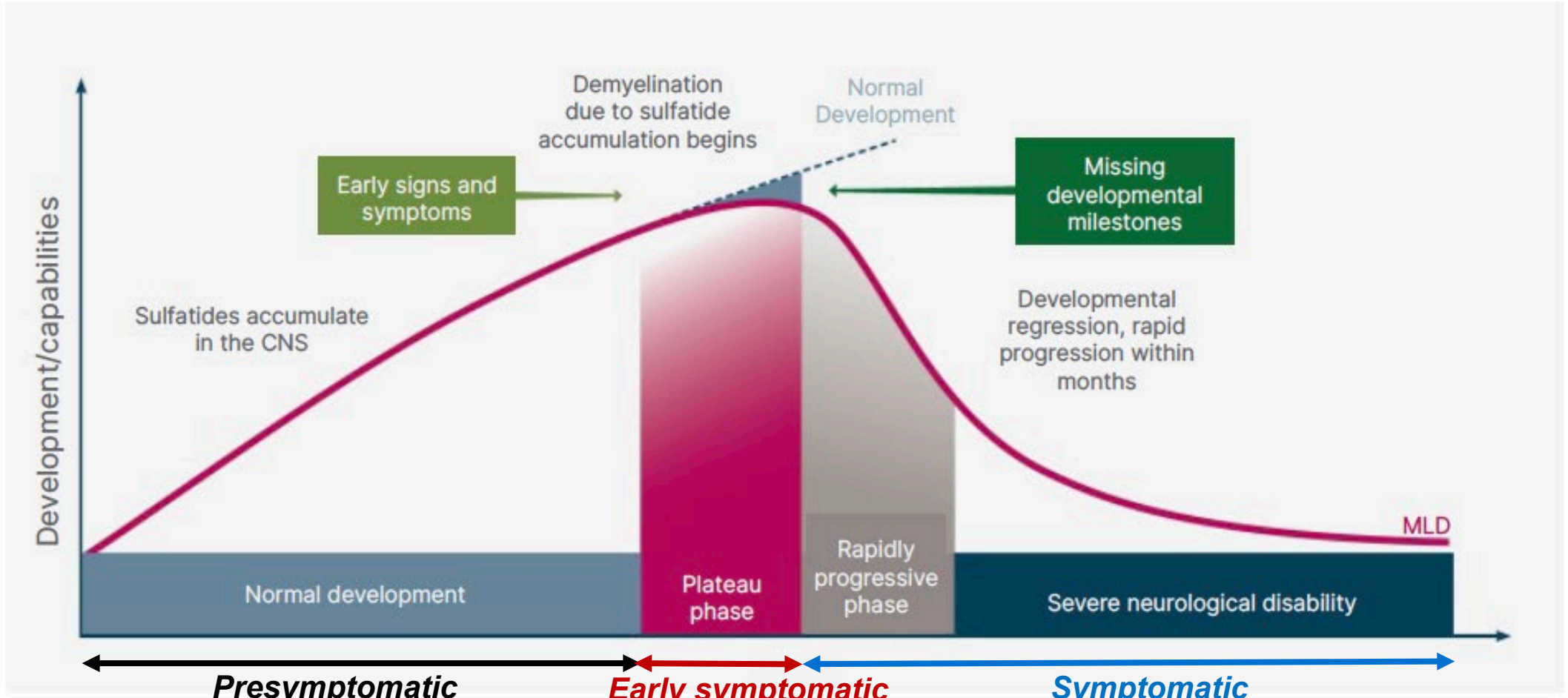
Metachromatic Leukodystrophy
Natural History



Campbell and Fumagalli, EMJ Neurol. 2022;10[1]:20-28.

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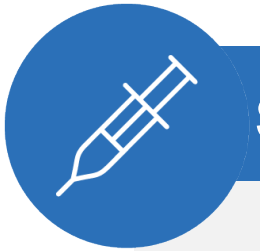
Metachromatic Leukodystrophy

Current Treatment

Supportive Care

- Physical & occupational therapy
- Nutrition support (G-tube)
- Wheelchair
- Symptomatic care (cough assist, oscillation device)
- Ventilator



Slow Disease Progression

- ? Hematopoietic stem cell transplant (HSCT)

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https://mldfoundation.org/mld-101-therapies.php

Insights from Discussions with Patients

- **Impact on caregivers and family**
  - Caregivers feel unprepared for hospital/ICU-level care children may need at home, especially at later stages of disease
  - Unaffected children also impacted – one parent always missing events, difficult to travel
  - Interpersonal relationship challenges may lead to separation and divorce
- **Financial impact**
  - One or both parents often need to leave the workforce
  - Insurance barriers/lack of coverage for nursing care, coverage of special diet, home modifications, etc.
- **Importance of newborn screening**
  - Possible gene therapy is most effective before symptoms of disease appear

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ICU: intensive care unit

Clinical Evidence

Populations for the Review

- Children with presymptomatic late infantile MLD (LI-MLD)
- Children with presymptomatic early juvenile MLD (EJ-MLD)
- Children with early symptomatic EJ-MLD
  - Able to ambulate independently (Gross Motor Function Classification for MLD [GFMC-MLD] score of ≤1)
  - Preserved cognition (intelligence quotient [IQ] score of ≥85).

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EJ: early juvenile, LI: late infantile, MLD: metachromatic leukodystrophy

Intervention

- Atidarsagene autotemcel (arsa-cel, Libmeldy™ in EU, OTL-200) compared with natural history cohort
- Treatment with arsa-cel includes:
  - Harvesting of patient's hematopoietic stem and progenitor cells
  - CD34+ cells transduced with lentiviral vector encoding ARSA cDNA
  - Patient undergoes bone marrow suppression with chemotherapy (busulfan conditioning)
  - Transduced cells are given back to patient through autologous stem cell transplantation

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ARSA: arylsulfatase A

Overview of Key Studies

Trials	N	Population	Key Outcomes
Phase I/II	20	Children with disease onset <7 years old • Presymptomatic LI-MLD • Presymptomatic EJ-MLD • Early symptomatic EJ-MLD	• Overall survival • Motor function (GMFM-88, GFMC-MLD) • Cognitive function • ARSA activity
Phase II	10	Same as Phase I/II study	• Same as Phase I/II study
Expanded Access Frameworks	3	Early onset MLD patients with similar enrollment criteria to clinical trials	• Similar endpoints to those in the primary study
Compassionate Use Programs	6		

ARSA: arylsulfatase A, GMFM: gross motor function measure, MLD: metachromatic leukodystrophy, N: total number

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Baseline Characteristics

Arms	Presymptomatic LI-MLD		Presymptomatic EJ-MLD	Early Symptomatic EJ-MLD	Overall EJ-MLD
	Arsa-cel	Natural History	Arsa-cel	Arsa-cel	Natural History
N	18	26	8	9	17
Male, n	13	12	6	6	9
Follow-up, median years (range)	6.1 (2.4-11)	4.4 (0.6-18.9)	3.3 (1.1-8.4)	7.2 (0.6-9.2)	5.6 (0.4-20.7)
Age at gene therapy or first contact, median	10.3 months	18.8 months	16.1 months	66.7 months	52.6 months
Baseline GMFM-88, mean	47.2	Not recorded	72.0	92.4	Not recorded

EJ-MLD: early juvenile MLD, GMFM: Gross Motor Function Measure, LI-MLD: late-infantile MLD

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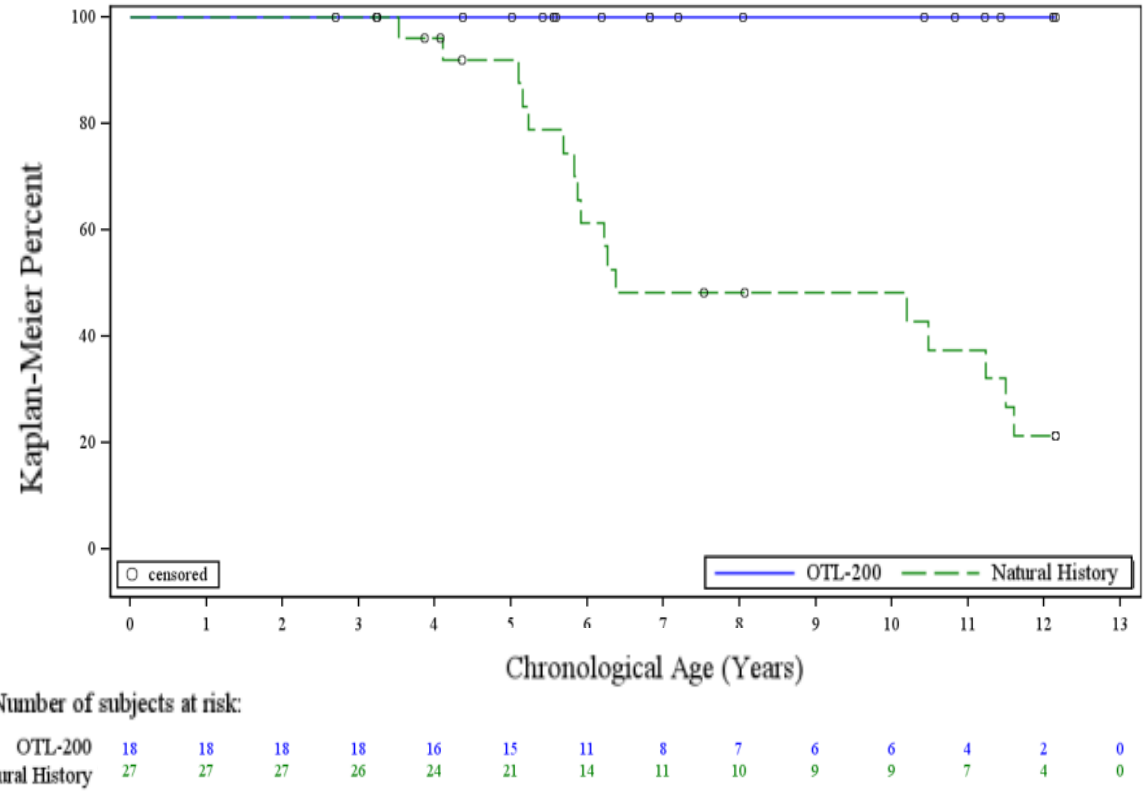
Overall Survival – Presymptomatic Patients

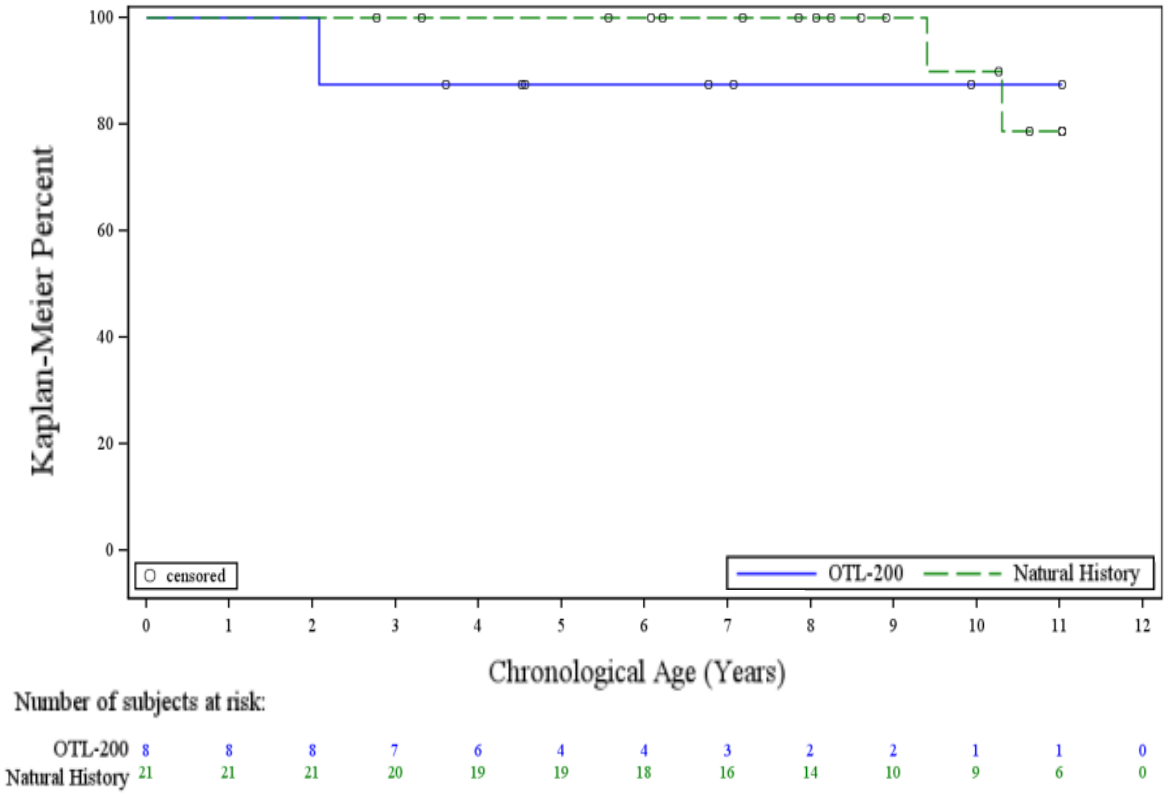
Late infantile



Number of subjects at risk:

OTL-200	18	18	18	18	16	15	11	8	7	6	6	4	2	0
Natural History	27	27	27	26	24	21	14	11	10	9	9	7	4	0

Early juvenile



Number of subjects at risk:

OTL-200	8	8	8	7	6	4	4	3	2	2	1	1	0
Natural History	21	21	21	20	19	19	18	16	14	10	9	6	0

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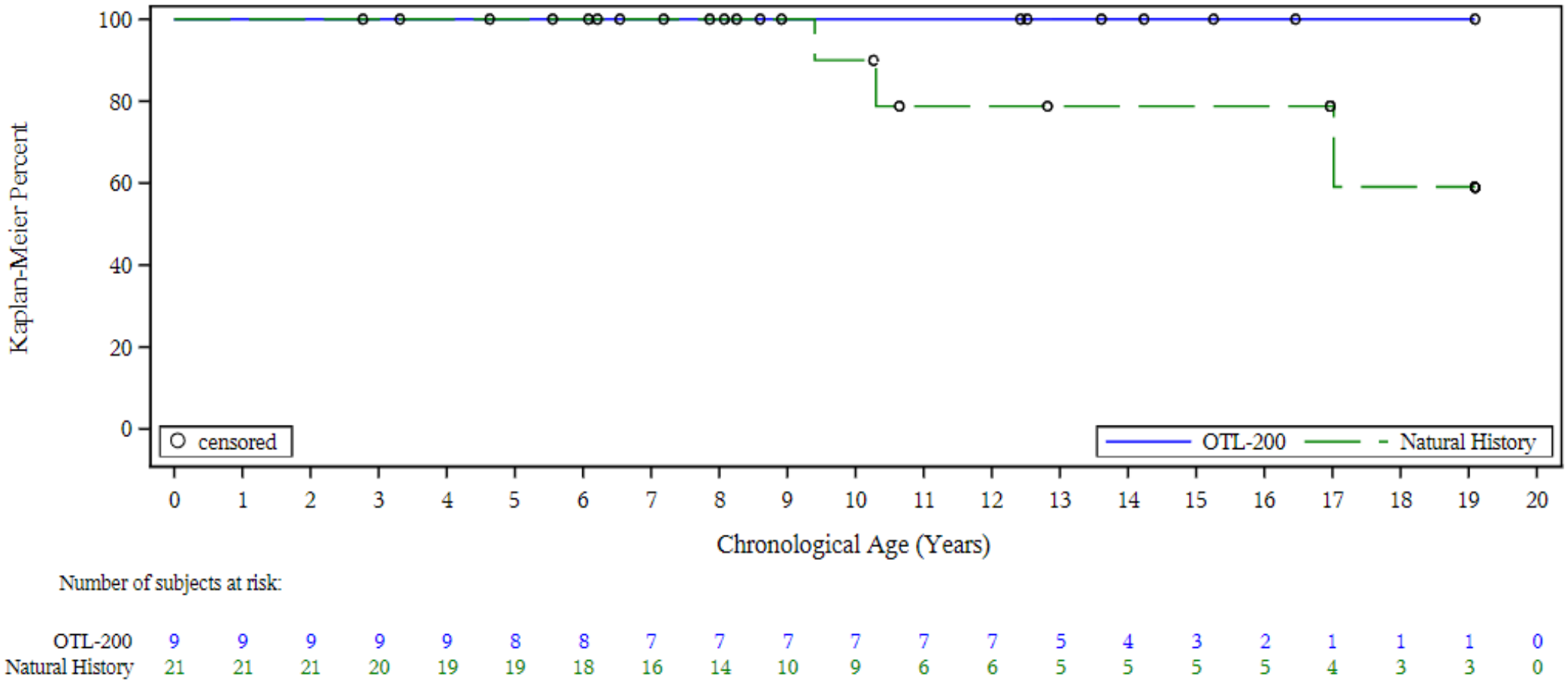
Fumigalli et al, Lancet 2022;399(10322):372-383

Overall Survival: Early Symptomatic EJ-MLD



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Fumigalli et al, Lancet 2022;399(10322):372-383

Gross Motor Function Measure (GMFM-88)

Arms	Presymptomatic LI-MLD		Presymptomatic EJ-MLD		Early symptomatic EJ-MLD	
	Arsa-cel	Natural History	Arsa-cel	Natural History	Arsa-cel	Natural History
Year 2						
N Evaluated	16	11	7	8	9	13
GMFM Total Score, Median	81.55	4.80	92.71	46.96	88.47	39.58
Treatment Difference	76.75		45.75		48.89	
Year 5						
N Evaluated	7	9	2	8	3	7
GMFM Total Score, Median	87.92	1.51	100	8.09	48.36	2.29
Treatment Difference	86.41		91.91		46.07	

[Scores range from 0 to 100 with a higher score indicating better performance]

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ARSA Activity Levels

- ARSA activity levels increased in all groups to normal or supranormal levels after treatment with arsa-cel.
- None of treated patients (N=35) had ARSA activity level in the peripheral blood cells below the reference range after up to 11 years of follow-up.

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ARSA: arylsulfatase A

Cognitive Function and Additional Endpoints

- Cognitive function was preserved in almost all treated patients compared to severe cognitive decline in patients in the natural history cohort.
- The majority of patients in the treated presymptomatic LI-MLD (17/18) and EJ-MLD (7/8) remained in GFMC-MLD stages 0-2.
- None of the trials collected data on health-related quality of life.

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EJ: early juvenile, GFMC: gross motor function classification, LI: late infantile, MLD: metachromatic leukodystrophy

Harms

- All patients had grade 3 or 4 adverse events, mainly from busulfan conditioning (febrile neutropenia, stomatitis)
- Of patients who had 7.5 years of follow-up:
  - Half had gait disturbance and one-third had motor dysfunction related to MLD progression
  - 15% of patients developed anti-ARSA antibodies
  - 1 death related to adverse event (presymptomatic EJ-MLD)

ARSA: arylsulfatase A, MLD: metachromatic leukodystrophy

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Controversies and Uncertainties

- Small, single arm study compared to a natural history cohort
- Unknown long-term durability and long-term harms
- Chance of disease progression after treatment
  - Two additional deaths in early symptomatic EJ-MLD patients in early stage of trial (excluded from analytic cohort)
- Chance of busulfan conditioning regimen hastening disease progression

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ARSA: arylsulfatase A

Potential Other Benefits and Contextual Considerations

- Currently no effective disease-modifying treatments for children with early onset MLD
- Children typically die during childhood; effective disease-modifying therapy would have a dramatic lifetime impact
- Caregiving impact of MLD is extremely high (work, physical/emotional impact, family impact)
- Effective treatment could change healthcare “infrastructure” in terms of earlier and better recognition of disease (e.g., newborn screening)

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MLD: metachromatic leukodystrophy

Public Comments Received

- Lack of access to an effective therapy should be considered harm

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ICER Evidence Ratings for Arsa-cel vs. Usual Care

Population	Evidence Rating
Presymptomatic LI-MLD	A
Presymptomatic EJ-MLD	A
Early symptomatic EJ-MLD	B+

EJ: early juvenile, LI: late infantile, MLD: metachromatic leukodystrophy

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Summary

- Early onset MLD is a rare but devastating disease
- Treatment for presymptomatic LI- and EJ-MLD prevents onset or delays progression of disease, extends survival with normal or near normal cognitive and motor function
- Benefit of treatment in early symptomatic EJ-MLD is smaller and less certain
  - Children do not recover function previously lost and more rapid progression prior to stabilization is possible
- Question remains regarding the durability and long-term harms of arsa-cel

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EJ: early juvenile, LI: late infantile, MLD: metachromatic leukodystrophy

Questions?

Atidarsagene Autotemcel: Effectiveness and Value

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Disclosures:

Financial support was provided to the University of Washington and Pittsburgh from the Institute for Clinical and Economic Review.

Drs. Suh and Carlson have no conflicts to disclose defined as more than $10,000 in health care company stock or more than $5,000 in honoraria or consultancies relevant to this report during the previous year from health care technology manufacturers or insurers.

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Objective

Estimate the lifetime cost-effectiveness of arsa-cel

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Methods in Brief

Methods Overview

- **Model**: Markov model
- **Setting**: United States
- **Perspective**: Health Care Sector and Modified Societal Perspectives
- **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; cost per equal value LYs gained (evLY)

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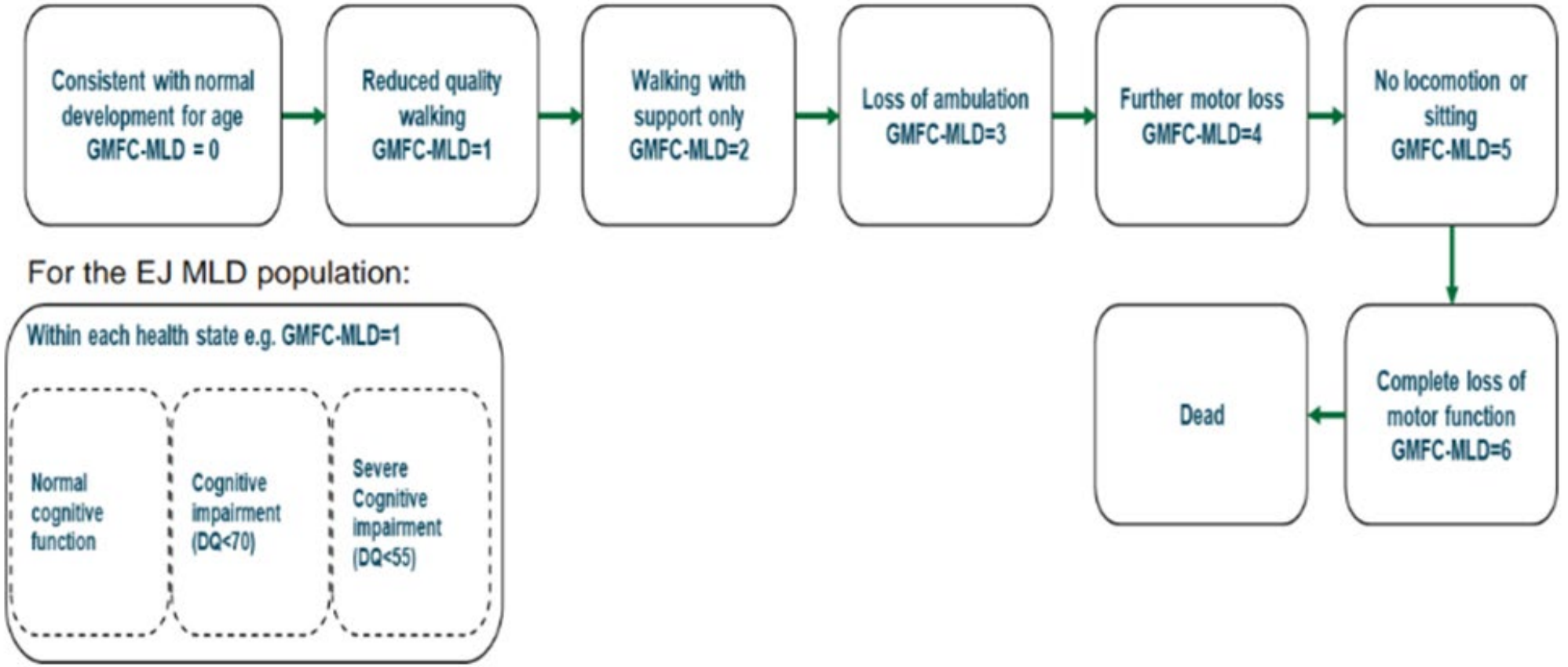
Model Schematic



DQ: Developmental Quotient, GMFC: Gross Motor Function Classification, MLD: Metachromatic Leukodystrophy

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Model Characteristics

- Target population: three subtypes of MLD
  - Presymptomatic LI-MLD
  - Presymptomatic EJ-MLD
  - Early symptomatic EJ-MLD

EJ: early juvenile; LI: late infantile; MLD: metachromatic leukodystrophy

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Key Model Inputs: Usual Care Mean Time to Transition (Months)

Presymptomatic Late Infantile

GMFC-MLD Transitions	Usual Care
From 0 to 1	3.32
From 1 to 2	4.22
From 2 to 3	3.53
From 3 to 4	3.53
From 4 to 5	3.53
From 5 to 6	10.10
From 6 to death	57.68

GMFC: Gross Motor Function Classification, MLD: Metachromatic Leukodystrophy

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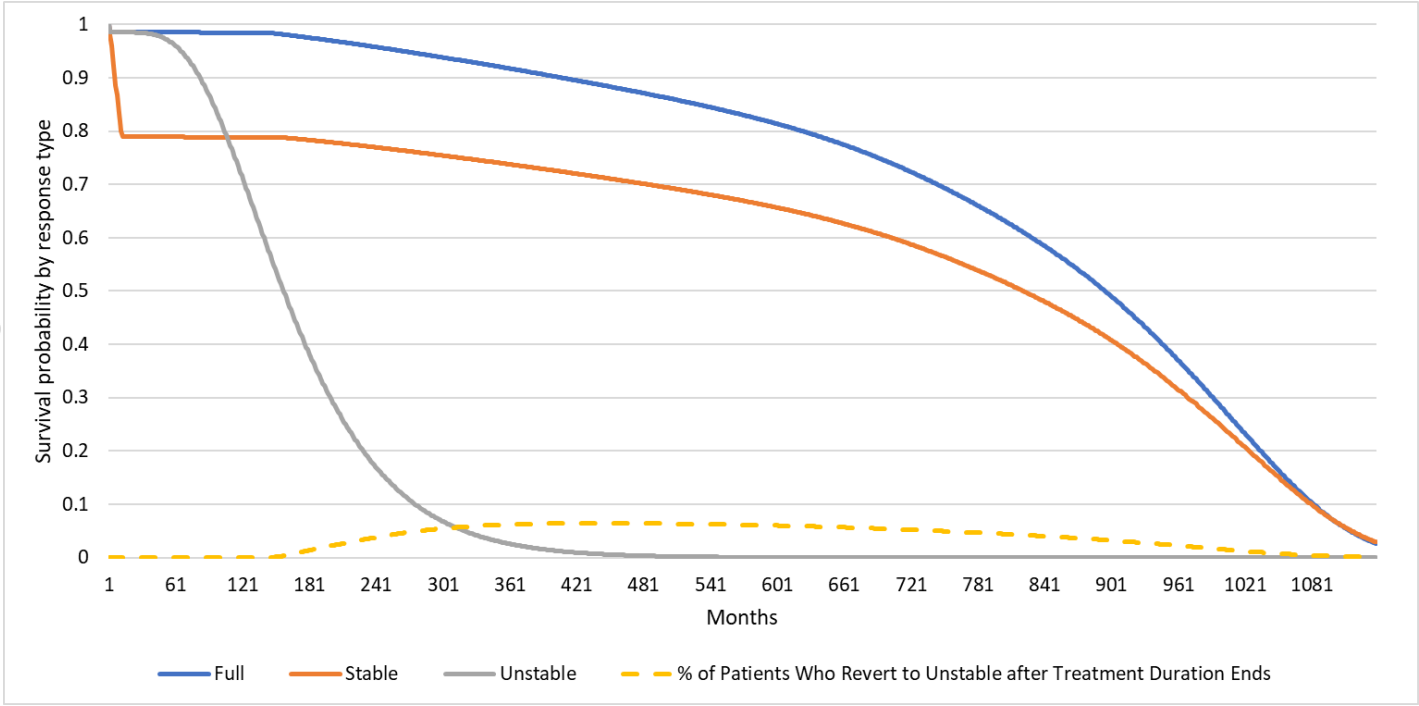
Key Model Inputs: Arsa-cel Transition Probabilities

Treatment effect is based on:

- Response type (trial data)
  - Full response
  - Stable partial response
  - Unstable partial response
- Disease stabilization (12 years, trial data)
- Post stabilization disease progression
  - 0.02% per month transition to unstable partial (prior ICER gene therapy reports)
  - Leads to 9.2% of full or partial responders experiencing disease progression by age 50

Presymptomatic Late Infantile



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Additional Model Assumptions

- Patients can only become progressively worse (i.e., move to a higher GMFC-MLD state)
- Patients can only die from GMFC-MLD state 6
- A 1.4% risk of death from infusion work for gene therapy in first model cycle

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Key Model Inputs: Treatment Costs

Cost	Value	Notes
Arsa-cel	$2,800,000	Placeholder price based on Norwegian Krone (NOK) 30,074,576, converted to US$2,800,240; one time cost
Arsa-cel Administration	$171,000	Includes costs for leukapheresis (cell harvesting), hospitalization and busulfan (conditioning), autologous bone marrow transplantation, follow-up related to autologous transplantation; one time cost

Arsa-cel: atidarsagene autotemcel

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Key Model Inputs: Health Care Sector Costs (Monthly)

Cost	Value	Notes
GFMC-MLD 0	$296	Most costs attributable to medical tests and visits
GMFC-MLD 1	$1,015	
GMFC-MLD 2	$1,912	
GMFC-MLD 3	$6,171	Greatest costs due to hospitalizations, daily nursing care, and healthcare equipment
GMFC-MLD 4	$7,435	
GMFC-MLD 5	$7,981	
GMFC-MLD 6	$20,058	

GMFC: Gross Motor Function Classification, MLD: metachromatic leukodystrophy

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Key Model Inputs: Indirect Costs (Monthly)

Cost	Value	Notes
Caregiver Loss of Income		Estimated from survey responses from 10 US caregivers of patients with MLD
GMFC-MLD 1 and 2	$83	
GMFC-MLD 3 and 4	$2,405	
GMFC-MLD 5 and 6	$4,019	
Out of Pocket Costs		
GMFC-MLD 1 and 2	$13	
GMFC-MLD 3 and 4	$503	
GMFC-MLD 5 and 6	$121	

GMFC: Gross Motor Function Classification; MLD: metachromatic leukodystrophy, US: United States

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Key Model Inputs: Utilities

	Late Infantile
GFMC-MLD 0	Age adjusted general population
GMFC-MLD 1	0.71
GMFC-MLD 2	0.44
GMFC-MLD 3	-0.04
GMFC-MLD 4	-0.13
GMFC-MLD 5	-0.20
GMFC-MLD 6	-0.27

GMFC: Gross Motor Function Classification, MLD: metachromatic leukodystrophy

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Key Model Inputs: Caregiver Disutilities

GMFC-MLD State	Caregiver disutility
0	0
1	-0.02
2	-0.027
3	-0.0675
4	-0.108
5	-0.135
6	-0.189

GMFC: Gross Motor Function Classification, MLD: metachromatic leukodystrophy

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Results

Base-Case Results

Drug	Drug Cost	Total Cost	QALYs	evLYs	LYs
Health Care Sector Perspective					
Arsa-cel	$2,800,000*	$3,493,000	18.32	20.94	25.66
Usual care	$0	$1,104,000	-0.51	-0.51	7.44
Incremental Results	$2,800,000	$2,389,000	18.83	21.45	18.22
Modified Societal Perspective					
Arsa-cel	$2,800,000*	$3,607,000	17.78	20.94	25.66
Usual care	$0	$1,383,000	-1.49	-1.49	7.44
Incremental Results	$2,800,000	$2,225,000	19.26	22.43	18.22

Arsa-cel: atidarsagene autotemcel, evLY: equal-value of life-year, LY: life-year, QALY: quality-adjusted life-year
*Based on placeholder price

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Base-Case Incremental Results

Treatment	Comparator	Cost per QALY Gained*	Cost per evLY Gained*	Cost per LY Gained*
Health Care Sector Perspective				
Arsa-cel	Usual care	$127,000	$111,000	$131,000
Modified societal perspective				
Arsa-cel	Usual care	$115,000	$99,000	$122,000

Arsa-cel: atidarsagene autotemcel, evLY: equal-value of life-year, LY: life-year, QALY: quality-adjusted life-year
*Based on placeholder price

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Subtype-specific Incremental Results

Subtype	Cost per QALY Gained*	Cost per evLY Gained*	Cost per LY Gained*
Healthcare Sector Perspective			
Presymptomatic LI	$119,000	$100,000	$109,000
Presymptomatic EJ	$79,000	$79,000	$101,000
Early Symptomatic EJ	$245,000	$193,000	$267,000
Modified Societal Perspective			
Presymptomatic LI	$107,000	$88,000	$100,000
Presymptomatic EJ	$65,000	$65,000	$87,000
Early Symptomatic EJ	$246,000	$181,000	$267,000

EJ: early juvenile; evLY: equal-value of life-year, LI: late infantile; LY: life-year, QALY: quality-adjusted life-year
*Based on placeholder price

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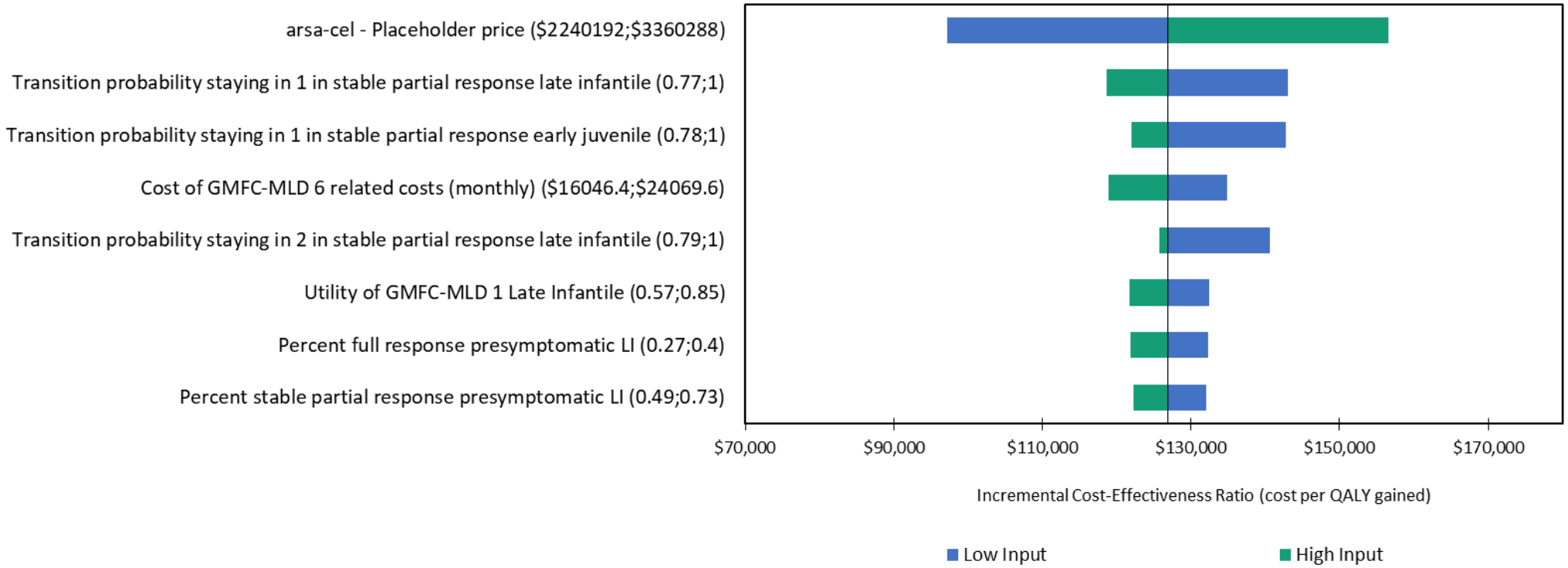
One-way Sensitivity Analyses



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Probabilistic Sensitivity Analysis

	Cost Effective at $50,000 per QALY Gained	Cost Effective at $100,000 per QALY Gained	Cost Effective at $150,000 per QALY Gained	Cost Effective at $200,000 per QALY Gained
Health Care Sector Perspective				
Arsa-cel	0%	0.01%	97.20%	100%
Modified Societal Perspective				
Arsa-cel	0%	4.1%	99.6%	100%

QALY: quality-adjusted life-year

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Scenario Analyses

	Cost per QALY Gained (Health Care Sector)	Cost per evLYG Gained (Health Care Sector)	Cost per QALY Gained (Modified Societal)	Cost per evLYG Gained (Modified Societal)
Rescaled Utility Estimates	$138,000	$121,000	$125,000	$108,000
Alternative Caregiver Disutilities	-	-	$121,000	$101,000

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

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Health Benefit Price Benchmarks (HBPBs)

Price Benchmarks for Arsa-cel

Intervention	Placeholder Price	Price at $100,000 Threshold	Price at $150,000 Threshold	Perspective
QALYs Gained				
Arsa-cel	$2,800,000	$2,294,000	$3,236,000	Health care sector
Arsa-cel	$2,800,000	$2,502,000	$3,465,000	Modified societal
evLYs Gained				
Arsa-cel	$2,800,000	$2,557,000	$3,629,000	Health care sector
Arsa-cel	$2,800,000	$2,818,000	$3,940,000	Modified societal

arsa-cel: atidarsagene autotemcel, evLY: equal-value of life-year, LY: life-year, QALY: quality-adjusted life-year

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Limitations

- Small sample
- Durability of treatment effect unknown
- Treatment response categories

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Comments Received

- Utilities that allow for negative values versus rescaled non-negative values
- Durability of treatment effect assumption
- Progression after stabilization period ends

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Conclusions

- Arsa-cel provides clinical benefit in terms of gains in QALYs, evLYs, and LYs over usual care from both the healthcare sector and modified societal perspectives
- At the currently assumed placeholder price, arsa-cel would be cost-effective at a commonly accepted threshold of $150,000 per QALY gained

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

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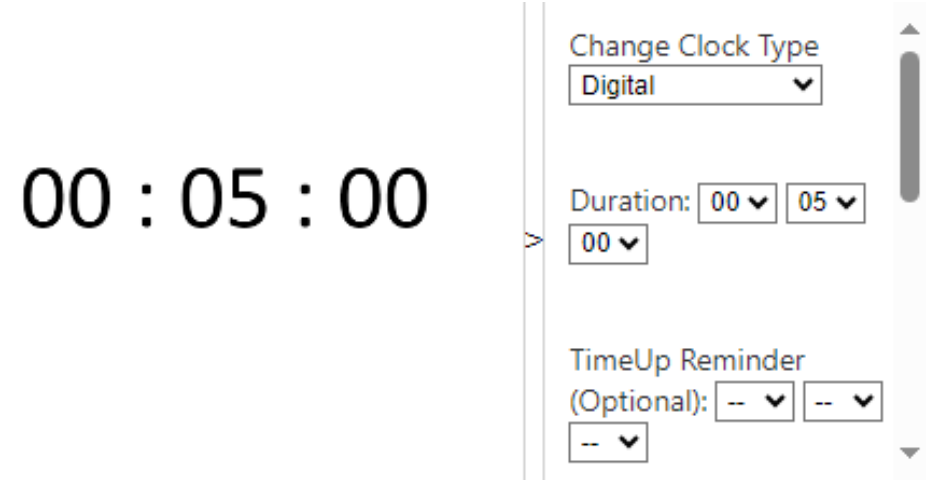
Questions?

Public Comment and Discussion

Kent Christopherson, Ph.D.
Executive Director & Head, Global Medical Affairs, Orchard Therapeutics

Conflicts of Interest:

- *Dr. Christopherson is a full-time employee of Orchard Therapeutics.*



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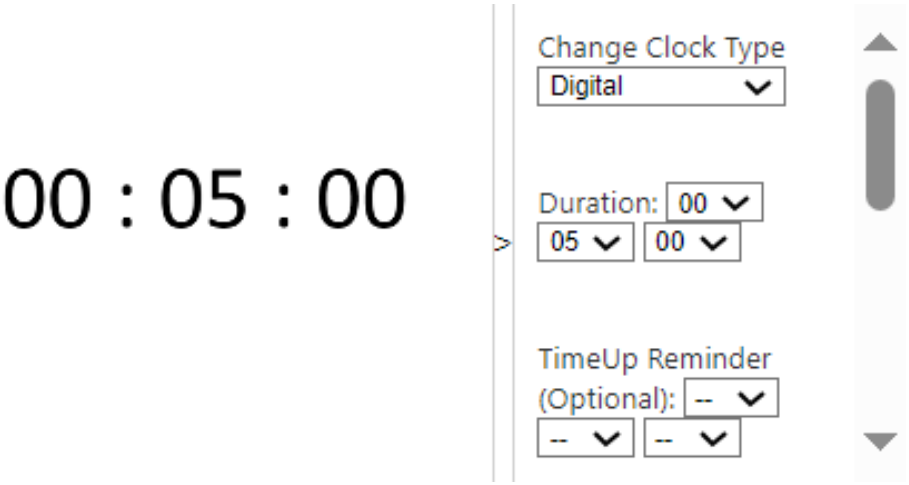
Maria Kefalas, Ph.D.
Founder, Cure MLD; Professor, Saint Joseph's University

Conflicts of Interest:

- *Cure MLD has received grants from Bluebird Bio, Homology Medicines, Orchard Therapeutics, Takeda Pharmaceuticals, and Passage Bio, Inc.*



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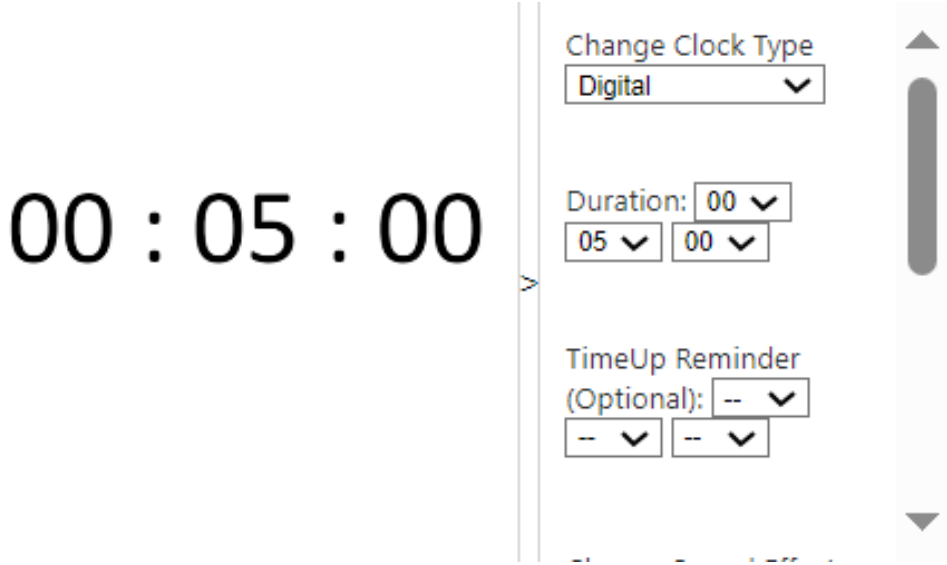
Victoria Rasberry
MLD Parent

Conflicts of Interest:

- *No conflicts to disclose.*



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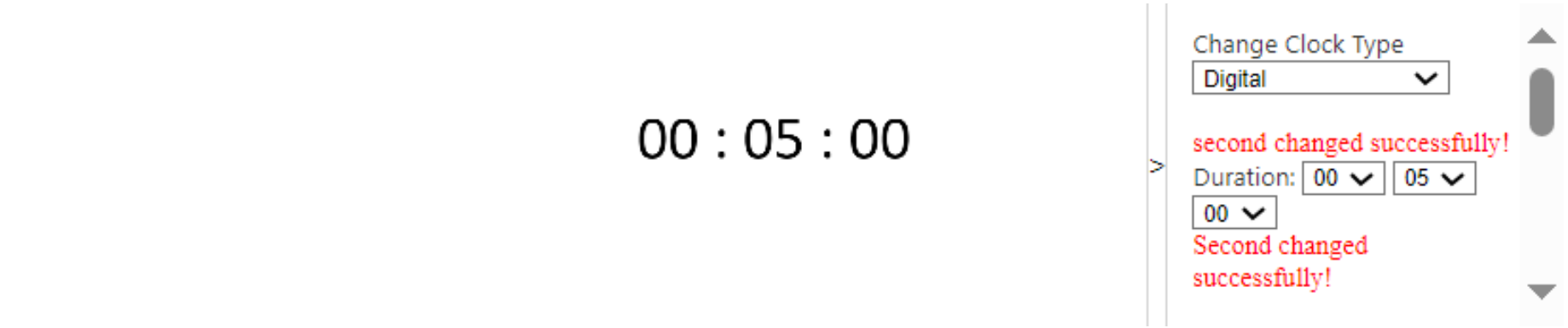
Dean Suhr, B.S.
President, MLD Foundation

Conflicts of Interest:

- *MLD Foundation has received sponsorships from various biopharma companies for their annual family conference.*
- *Mr. Suhr has equity interests such as individual stocks, stock options, or other ownership interests in excess of $10,000 in Orchard Therapeutics.*



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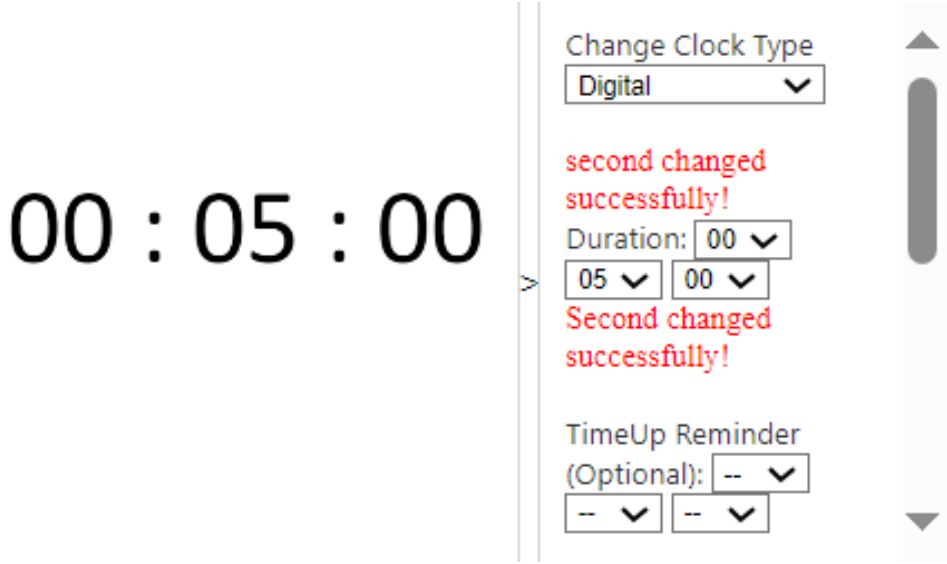
Amy Wright
MLD Parent

Conflicts of Interest:

- *No conflicts to disclose.*



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Lunch

Meeting will resume at 11:50 AM PT

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Voting Questions

Clinical Evidence Questions

slido

Patient Population: Children with presymptomatic late infantile MLD.

Is the currently available evidence adequate to demonstrate that the net health benefit of atidarsagene autotemcel (arsa-cel) is superior to that provided by usual care?

ⓘ Start presenting to display the poll results on this slide.

slido

Patient Population: Children with presymptomatic early juvenile MLD.

Is the currently available evidence adequate to demonstrate that the net health benefit of arsa-cel is superior to that provided by usual care?

ⓘ Start presenting to display the poll results on this slide.

slido

Patient Population: Children with early symptomatic early juvenile MLD.

Is the currently available evidence adequate to demonstrate that the net health benefit of arsa-cel is superior to that provided by usual care?

ⓘ Start presenting to display the poll results on this slide.

Contextual Considerations and Potential Other Benefits or Disadvantages Questions

Patient Population: Children with presymptomatic late infantile MLD or presymptomatic early juvenile MLD

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

slido

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

ⓘ Start presenting to display the poll results on this slide.

slido

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

ⓘ Start presenting to display the poll results on this slide.

Patient Population: Children with presymptomatic late infantile MLD or presymptomatic early juvenile MLD

What are the relative effects of arsa-cel versus usual care on the following outcomes that inform judgment of the overall long-term value for money of arsa-cel?

slido

Patients’ ability to achieve major life goals related to education, work, or family life

ⓘ Start presenting to display the poll results on this slide.

slido

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

ⓘ Start presenting to display the poll results on this slide.

slido

Society’s goal of reducing health inequities

ⓘ Start presenting to display the poll results on this slide.

Other: The entire “infrastructure” of care, including effects on screening for affected patients, the awareness of clinicians, and the dissemination of understanding about the condition, that may revolutionize how patients are cared for in ways that extend beyond the treatment itself

slido

Entire infrastructure of care that may revolutionize how patients are cared for in ways that extend beyond the treatment itself

ⓘ Start presenting to display the poll results on this slide.

Long-Term Value for Money Question

Given 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 at current pricing with arsa-cel versus usual care?

slido

What is the long-term value for money of treatment at current pricing with arsa-cel versus usual care?

ⓘ Start presenting to display the poll results on this slide.

Break

Meeting will resume at 1:00 PM PT

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Policy Roundtable

Policy Roundtable Participant	Conflict of Interest
Francesca Fumagalli, M.D, Ph.D., Neurologist, Pediatric Immunohematology Unit and Department of Neurology, IRCCS San Raffaele Hospital, Milan	Dr. Fumagalli is a sub investigator of clinical trials NCT01560182 and NCT03392987 and PI of clinical trial NCT04283227 using OTL-200 sponsored by Orchard Therapeutics. Dr. Fumagalli has received less than $5,000 in honoraria from Orchard Therapeutics and Takeda.
Stephen Jung, Pharm.D., Principal Pharmacist, Blue Shield of California	Stephen is a full-time employee of Blue California.
Maria Kefalas, Ph.D., Founder, Cure MLD; Professor, Saint Joseph's University	Cure MLD has received grants from Bluebird Bio, Homology Medicines, Orchard Therapeutics, Takeda Pharmaceuticals, and Passage Bio, Inc.
Julia Mahler, Pharm.D., Clinical Pharmacist, IPD Analytics	Julia is a full-time employee of IPD Analytics.
Paul Orchard, M.D., Director of the Inherited Metabolic and Storage Disease Program, Professor of Pediatric Blood and Marrow Transplantation and Cellular Therapy, University of Minnesota	Dr. Orchard's team offers expanded access to OLT-200 in association with Orchard Therapeutics for specific patients. Dr. Orchard has received less than $5,000 in honoraria or consultancies from Orchard Therapeutics.
Francis Pang, MBA, SVP, Global Market Access & International Geographic Expansion, Orchard Therapeutics	Francis is a full-time employee of Orchard Therapeutics.
Teryn Suhr, R.N., Executive Director, MLD Foundation	The MLD Foundation has received sponsorships from various biopharma companies for their annual family conference. Mrs. Suhr has equity interests such as individual stocks, stock options, or other ownership interests in excess of $10,000 in Orchard Therapeutics.

CTAF Council Reflections

Next Steps

- Meeting recording posted to ICER website next week
- Final Report published on or around October 30, 2023
    - Includes description of CTAF votes, deliberation, policy roundtable discussion
- Materials available at: https://icer.org/assessment/metachromatic-leukodystrophy-2023/#timeline

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Adjourn

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