Fundamental Rights: Access to Treatment
February 2024 Roundtable
Meeting Summary

Contents

Executive Summary

On February 8, 2024, a multi-stakeholder group, representing various communities within the International Alliance of ALS/MND Associations' network, gathered for a Roundtable focused on the first of the Alliance's Fundamental Rights for Persons Living with ALS/MND: Access to Treatment.

Not all countries are able to meet the basic needs of people living with ALS/MND or there may be limited availability and access to treatments. Even in countries with more advanced healthcare systems, within the current access environment, each country or geography has its own processes for investing in, approving, and making treatments available.

The Roundtable discussion was designed to help provide an understanding of the challenges regions/jurisdictions face in getting access to clinical trials and approved drugs, and what tools they need to help with their efforts.

The meeting included an opening plenary, and two group discussions. During the plenary session, participants heard a series of brief expert presentations designed to describe the full continuum of access to treatment, from laboratory and pre-clinical research to access to clinical trials, regulatory approval, coverage, and access.

Attendees

Meeting participants included representatives from multiple global ALS/MND organizations, members of the Alliance's staff and PALS and CALS Advisory Council (PCAC), industry officials and invited expert speakers. All sessions were facilitated by Wendy Selig, Founder and CEO of WSCollaborative, and sponsorship support for the Roundtable was provided by Amylyx, Cytokinetics and MT Pharma America.

Attendee Roster - Discussion Group 1			
Last Name	**First Name**	**Affiliation**	**Country**
Aquino	Irene	Amylyx	USA
Arblaster	Kielan	MOTOR NEURONE DISEASE ASSOCIATION (MNDA UK)	England, Wales, N Ireland (UK)
Barajas	Raquel	Fundación Luzón	Spain
Bayerlein	Nancy	Mitsubishi Tanabe Pharma	USA
Bulat	Allison	Northeast ALS Consortium (NEALS)	USA
Conte	Silverio	Associazione conSLAncio Onlus (Italy)	Italy
Crespo	Cristina	Sanofi	Spain
Cummings	Catherine	The International Alliance of ALS/MND Associations	Canada
Dave	Kuldip	THE ALS ASSOCIATION (ALSA)	USA
de Majo	Martina	The International Alliance of ALS/MND Associations	Italy
DiMartino	Jennifer	ALS ONE	USA
Dupont	Melissa	Sanofi	USA

Filic	Ivona	Mitsubishi Tanabe Pharma	USA
Fitzgibbon	Naomi	IRISH MOTOR NEURONE DISEASE ASSOCIATION (IMNDA)	Ireland
Großkreutz	Julian	EU Coalition	Germany
Henning	Franclo	Motor Neurone Disease/ALS Association of South Africa	South Africa
Hockensmith	Tanner	THE ALS ASSOCIATION (ALSA)	USA
Kaya	Alper	ALS/MND Association Türkiye	Turkey
Mabe	Jessica	The International Alliance of ALS/MND Associations	Colombia
Marie	Anne	LES TURNER ALS FOUNDATION	USA
Moore	Tammy	ALS Society of Canada	Canada
Pasinelli	Piera	Jefferson Weinberg ALS Center	USA
Peña	Martha	Roosevelt Institute	Colombia
Phatak	Hemant	Amylyx	USA
Reviers	Evy	ALS Liga Belgium	Belgium
Ruiz	Orlando	ASOCIACIÓN COLOMBIANA DE ESCLEROSIS LATERAL AMIOTRÓFICA (ACELA)	Colombia
Sane	Hemangi	ASHA EK HOPE FOUNDATION	India
Schmitz	Robert	Motor Neurone Disease Association Singapore	Singapore
Selig	Wendy	Facilitator	USA
Sigurdsson	Gudjon	MND Iceland	Iceland
Simon	Julia	The International Alliance of ALS/MND Associations	Canada
St. Onge	Louise	Mitsubishi Tanabe Pharma	Canada
Stephens	Leigh	Société de la SLA du Québec | ALS Society of Quebec	Canada
Tran	Nguyen	ALS Vietnam	Vietnam
Ulgenalp	Ilayda	ALS Society of Canada	Canada
van der lit	Angelique	ALS Patiëntenvereniging	Netherlands
Vande Velde	Christine	Robert Packard Center for ALS Research at John Hopkins	Canada
Virgo	Bruce	PCAC	Scotland
Webb	Lauren	LES TURNER ALS FOUNDATION	USA
Wicks	Paul	Digital Health	UK

Attendee Roster - Discussion Group 2			
Last Name	**First Name**	**Affiliation**	**Country**
Bulat	Allison	Northeast ALS Consortium (NEALS)	USA
Calderón	Andrea del Pilar	ELATAM	Colombia

Cummings	Catherine	The International Alliance of ALS/MND Associations	Canada
de Majo	Martina	The International Alliance of ALS/MND Associations	Italy
Dupont	Melissa	Sanofi	USA
Gardner	Mike	ITAC	USA
Liu	Qing	SAC	China
Mabe	Jessica	The International Alliance of ALS/MND Associations	Colombia
Manuel	Machelle	Amylyx	USA
Peña	Martha	Roosevelt Institute	Colombia
Phatak	Hemant	Amylyx	USA
Schmitz	Robert	Motor Neurone Disease Association Singapore	Singapore
Selig	Wendy	Facilitator	USA
Sethi	Nadia	ALS THERAPY DEVELOPMENT INSTITUTE	USA
Sklavenitis	Leanne	PCAC	Australia
Stephens	Leigh	Société de la SLA du Québec | ALS Society of Quebec	Canada
Thomas	Gethin	MND Australia	Australia
Tortorella	Silvia	INSTITUTO PAULO GONTIJO (IPG)	Brazil
Tremblay	Jennifer	Sanofi	Canada
Vergara	Berta	Asociación Unidos para Apoyarte (AUPA)	Panama

Agenda

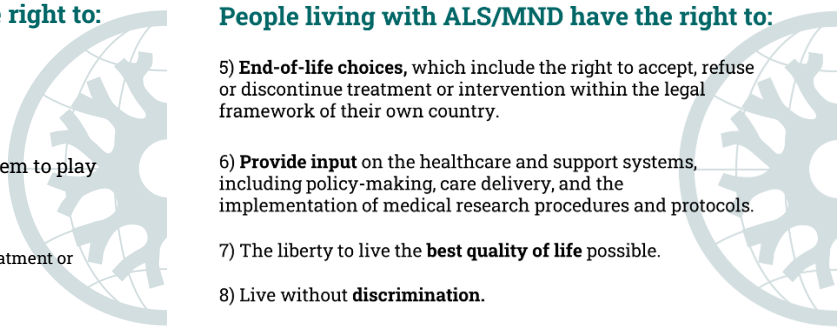
Agenda Detail	
Plenary: Tuesday February 8: 7:00-8:30am ET (New York)	
1. Contextual overview	
○ Fundamental rights	Cathy Cummings
○ Alliance´s position paper on "Access to treatments"	Calaneet Balas
2. PALS Perspective	Albert Koo
3. Laboratory Research & Pre- Clinical Studies	Dr. Christine Vande Velde, PHD
4. Clinical trials	Nicholas Earle
5. Regulatory review	Tammy Moore
6. Health Technology Assessment (HTA) Bodies	Hemant Phatak
7. Drug coverage / reimbursement process	Calaneet Balas
8. Patient Access	Julian Großkreutz & Evy Reviers
9. Questions	
10. Wrap up & Discussion group instructions	

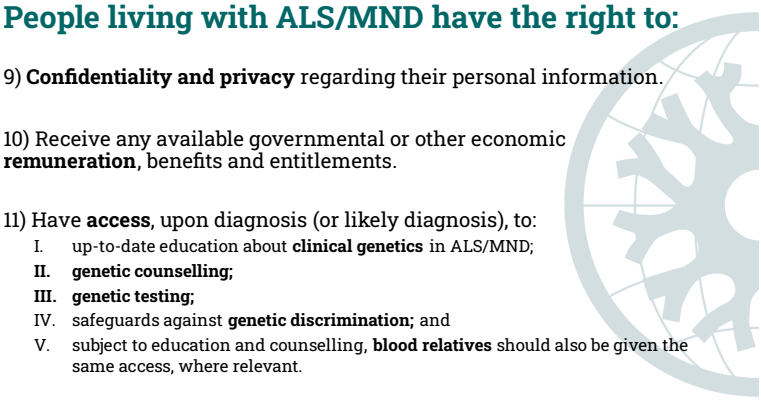
Group Discussion Virtual: Tuesday, October 18; Group 1: 9-10:30am ET: Group 2: 7-8:30pm ET
Debrief from Plenary
Facilitated Discussion: 1. What are the challenges your region/jurisdiction faces in getting access to treatments? You have 2-3 minutes to: ○ Describe the **top one** challenge in your area ○ If you had a magic wand to accomplish **one** solution, what would it be? 2. Is there anything missing in the list of approaches? Please refer to the document "Equitable access to therapies on a global scale", pages 5-7.
Wrap up and Next Steps

A summary of the discussion during the Access to Treatment Roundtable meeting are embedded in the document that follows.

Opening Comments

Alliance Executive Director **Cathy Cummings** and Chair **Calaneet Balas** provided the background and context for the Roundtable, which is the first of a series that will be focused on individual components of the Alliance's Fundamental Rights for People Living with ALS / MND. These include the right to the highest quality treatments, access to information and education, choices regarding end-of-life care, input into surrounding systems, living without discrimination, confidentiality, privacy, remuneration, and access to genetic counseling and testing.

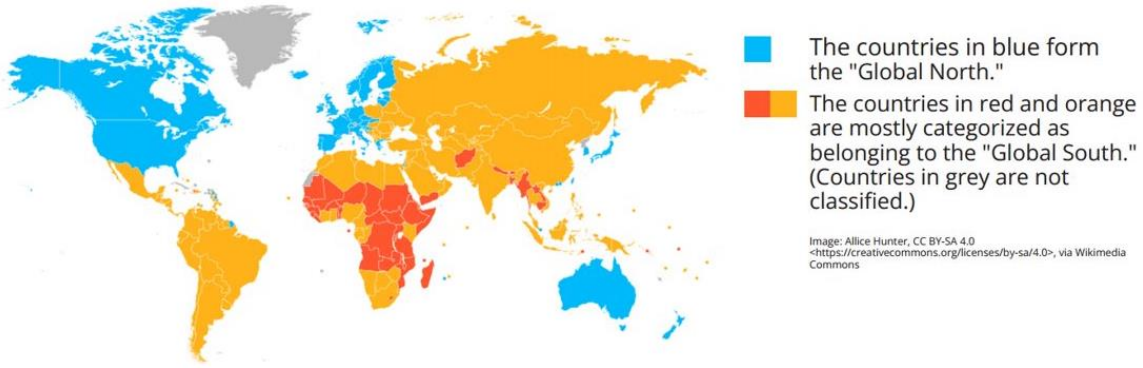




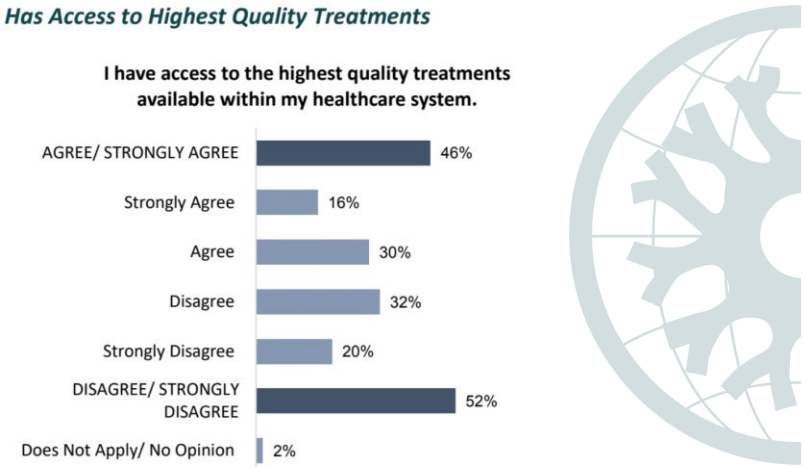
The Alliance surveyed its global constituents in 2021 and again in 2023, when almost 2000 participants in 54 countries responded. The 2021 survey provided an initial baseline from which the 2023 survey results could be evaluated.

The 2023 survey looked at the Global North and Global South. Note that many people use the term "developed" and "developing" nations, and various international agencies have other ways of grouping countries based on their defining characteristics with regard to socioeconomics and politics. The Alliance uses the concepts of Global North and Global South, which come from the United Nations. The division between the Global North and Global South is often used in discussions about global inequality and we believe they effectively illustrate the differences in the ALS/MND community.

Global North and South

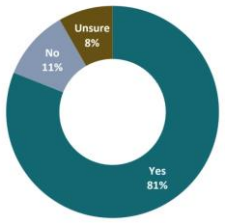


In 2023, fewer than half of the respondents (46%) felt their right to access the highest quality treatment is respected.

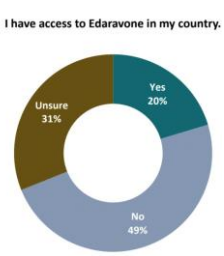


Responses on this and related questions were higher in the Global North of the world than the Global South, while English-speaking countries had higher positive responses than non-English-speaking countries regarding access to treatments. Results showed varying levels of perceived access to treatments approved for use in multiple parts of the world, with concerns about disparities and uncertainty in some regions.

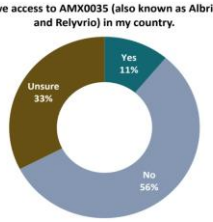
Has access to Riluzole



Has access to Edaravone

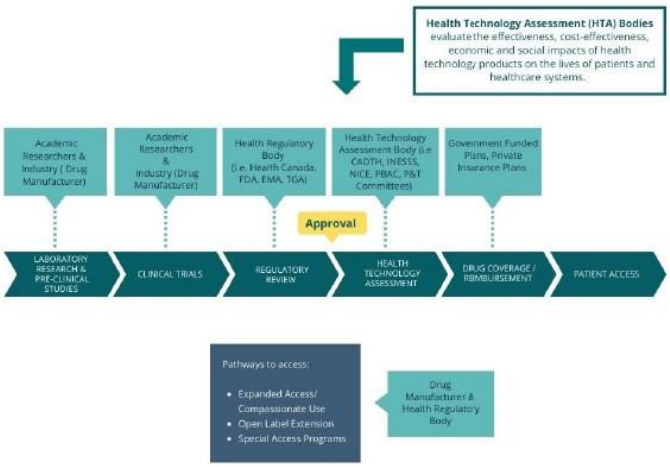


Has access to AMX0035 (also known as Albrioza and Relyvrio)



Factors influencing the perception of access included participation in clinical trials and access to specific treatments like AMX0035.

The Alliance has developed a position paper "Equitable Access to Therapies on a Global Scale," with the draft shared among all Roundtable participants prior to the meeting for their feedback. This document addresses global disparities in access, encourages collaboration, highlights barriers to treatment access, and underscores the importance of removing those barriers. The paper will serve as a platform for global collaboration and discussion, providing a foundation for advocacy to improve access to treatments for ALS / MND globally.

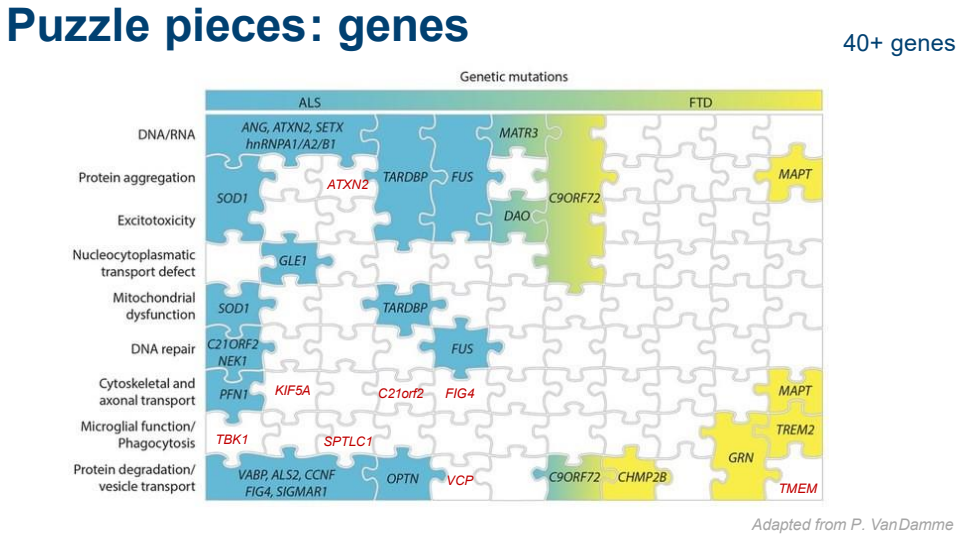


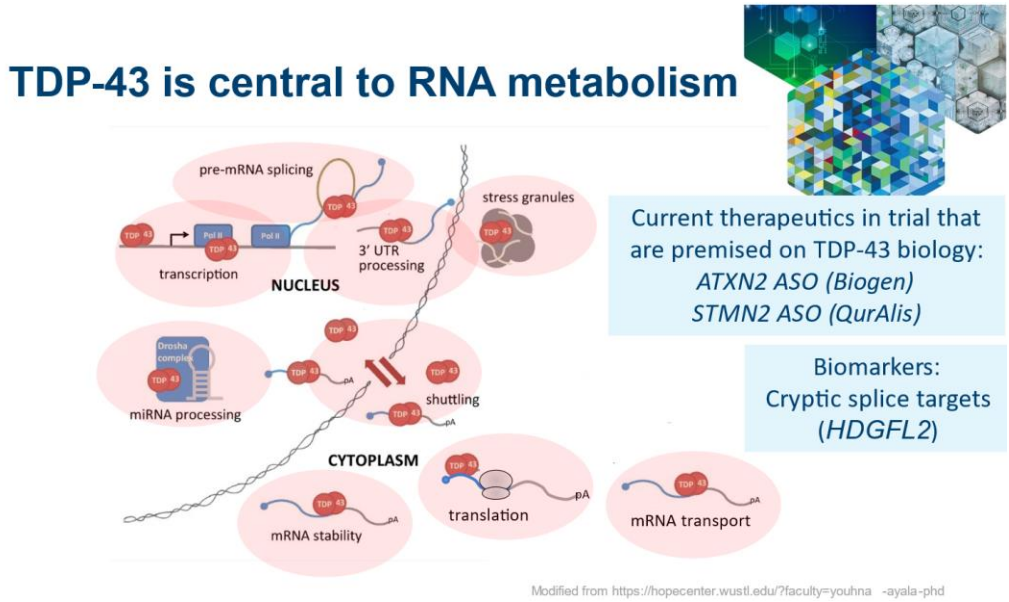
Albert Koo Tee Yih, a person living with ALS/MND from Malaysia, shared his perspective on challenges faced in his region, including high costs for approved drugs, financial burdens, and limited inclusion in clinical trials. Challenges identified include the high cost of approved drugs, financial constraints for patients, and limited inclusion in global clinical trials for people living with ALS/MND in regions like Malaysia. He emphasized the importance of addressing financial barriers and increasing participation from underrepresented regions in global clinical trials.

Expert Presentations:

Christine Van de Velde of The Packard Center for ALS Research provided a brief overview of the role of lab research and preclinical studies in ALS/MND drug discovery. She stressed that the guiding principle of research in this area is to understand the biology of ALS/MND to develop disease-modifying treatments and valid biomarkers. These biomarkers are crucial for assessing the effectiveness of treatments and tracking individual disease progression.

Genes play a significant role in ALS/MND research, with over 40 genes associated with the disease. Understanding the interplay of these genes and their pathways is crucial for identifying potential targets for drug discovery. TDP 43, for example, is a protein central to ALS/MND pathology. Its mis-localization is observed in about 97% of ALS/MND cases, making it a key target for research. TDP 43 is essential for RNA metabolism, influencing various processes, and is the basis for new therapeutics.

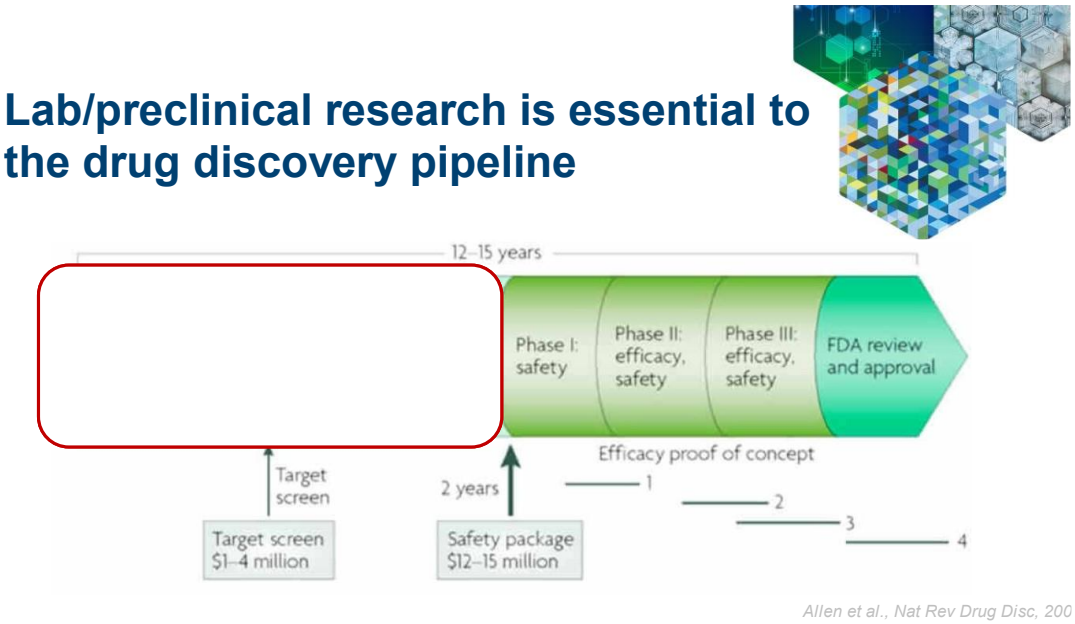




*Slides by Dr. Christine Vande Velde

The drug discovery process involves various phases such as research and development, preclinical studies, clinical trials, and review/approval. Academic and industrial labs focus on identifying targets for new therapies, screening compounds, and conducting in vitro and in vivo studies. Preclinical research in ALS/MND is global and collaborative. Researchers worldwide contribute to understanding ALS/MND biology, with various targets and therapies under pursuit. This reflects the complexity of the disease and underscores the need for multimodal therapies.

Dr. Van de Velde stressed that understanding the biology of the disease is crucial for developing effective therapies and biomarkers. Progress in this effort depends on ongoing investment in preclinical studies to continually fill the drug discovery pipeline.



*Slide by Dr. Christine Vande Velde

Nicholas Earle of the University of Chile described limitations of the healthcare landscape in Chile, where ALS/MND clinics are primarily initiated by individuals with a personal interest and there is a division between public and private systems. He also provided an overview of the Latin American Consortium (ELATAM) for the care, treatment, and research in ALS/MND and other motor neuron diseases. ELATAM aims to improve access to care and treatment for ALS/MND patients in Latin America, where there is a significant gap in resources and availability of treatments. He emphasized the challenges in providing access to treatments due to high costs, making it difficult for patients in some countries to afford essential medications.

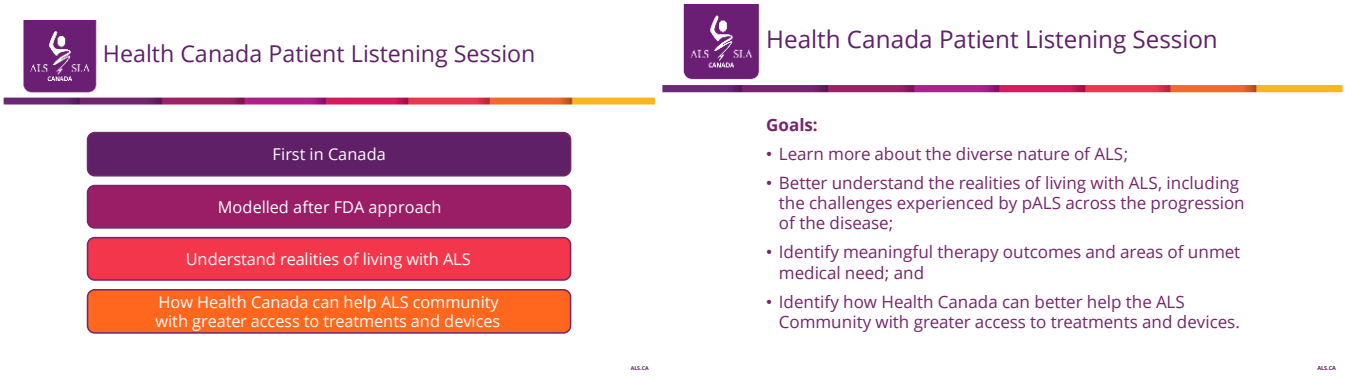
He also highlighted the need for increased participation in clinical trials in Latin America, citing the limited infrastructure and resources available and noting that participation in clinical trials should be a right for every patient and is essential for advancing the understanding and treatment of ALS/MND.

	Riluzole	Edaravone	Tofersen	Fenilbutirato de sodio/taurursodiol	Clinical trials concluded	Clinical trials actives
Uruguay	Partially available in the public system	-	-	-	-	-
	Not available by law or in the private system					
Cosa Rica	Available by law	-	-	-	-	-
Chile	Not available by law or in the private system. Available for purchase	-	-	-	Non-systematic sporadic recruitment	-
Colombia	Available by law	Vital not available until 2019	-	-	-	-
Perú	Not available by law or in the private system. Available for purchase	-	-	-	-	-
Argentina	Available by law	Available by law	-	-	Masitinib I-II, Acthar gel, Apelis	PTC utreloxastat
Guatemala	Available in the system for employees (Social Security)	-	-	-	-	-
Cuba	Partially available, very limited access	-	-	-	-	-
México	Available by law or in the private system. Available for purchase	-	-	-	-	-
Paraguay	Available in the system for employees (Social Welfare Institute). It is not available in the public system or to buy it	-	-	-	-	-
Brasil	Available by law	Partially available, very limited access	-	-		
Salvador	Partially available, very limited access	-	-	-	-	-

*Slide by Dr. Nicholas Earle

Tammy Moore of the ALS Society Canada discussed the evolution of access to therapies for the Canadian ALS/MND community, focusing on her efforts to engage with regulators. She emphasized the importance of building relationships and serving as a trusted source of information for regulators, helping them understand the needs of people living with ALS/MND. This is important early in the process of drug development, not just when a drug is in the final stages of approval.

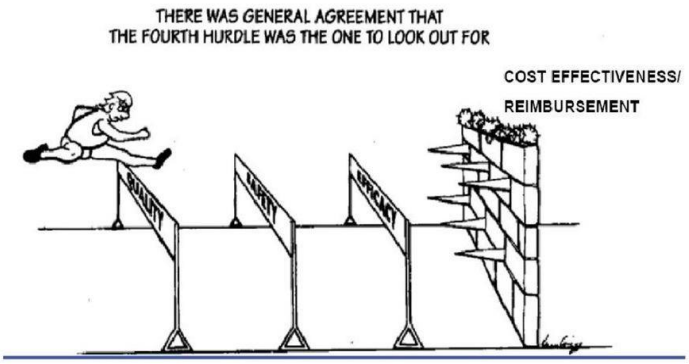
She shared examples of training sessions conducted for members of the ALS/MND community to help them understand the regulatory process so they could engage effectively, and described a recent listening session designed to educate regulators about the needs of the ALS/MND community. The outcomes of these initiatives include a better understanding by regulators, increased responsiveness to the needs of the ALS/MND community, and ongoing efforts to enhance access to treatments.



*Slides by Tammy Moore

Hemant Phatak of Amylyx described the Health Technology Assessment (HTA) process, emphasizing its role in determining the reimbursement and market access of approved therapies, noting that regulatory approval is just the beginning, and the real challenge in providing access lies in navigating the HTA process. He described HTA as the fourth hurdle for patients' access to therapies.

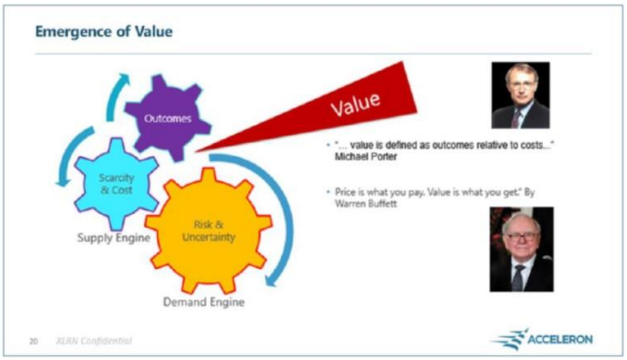
Reimbursement as a Fourth Hurdle



PAOs and people with lived experiences can help reduce the time required to scale the 4th hurdle

Source: https://www.slideserve.com/makani/health-technology-assessment

Determination of Value in the Era of Resource Constraints: Basis of Health Technology Assessment (HTA)



Car Buying Scenario…

- Do you buy for speed?
- Do you buy for luxury?
- Do you buy for financial?
- Do you buy for environment?
- Do you buy for safety?

Health technology assessment (HTA) is a formal, systematic research process designed to synthesize and evaluate the existing evidence for a medical treatment via multi-faceted assessment of the clinical, economic, ethical, legal, and societal perspectives that may be impacted by a new technology, procedure, drug, or process

Courtesy: Apperture LLC, for the source slide please contact ambi@apperturehealth.com

*Slides by Hemant Phatak

HTA involves a formal research process to evaluate the clinical, economic, ethical, legal, and societal aspects of a therapy. It is important to align the value perceptions of demand (governments/payers) and supply (pharmaceutical companies) sides for successful market access. There are three phases of HTA: Assessment, Appraisal, and Decision Making. Advocacy organizations can play a crucial role in educating HTA agencies about ALS/MND, influencing the assessment criteria, and participating in the appraisal phase.

There is increasing influence of HTA in global markets, particularly in Europe, where it is a well-established and utilized process. HTA has an impact on drug development strategies and the need for collaboration among advocacy groups, pharma companies, and HTA agencies. In the U.S., there is not a formal HTA process, but there will be more in this area given passage of the IRA (Inflation Reduction Act) and CMS (Centers for Medicare and Medicaid Services) beginning negotiation of drug prices. Access issues in one country reverberate in other countries and most of the HTA assessments become public once reimbursement is issued. It is an opportunity for patient advocacy organizations to influence the process in a subset of countries, so things become easier for other countries.

Processes Are Vastly Different from country to country

Market	Evaluation Criteria	Key Metrics
	• Cost effectiveness • Comparative clinical effectiveness and health-related factors	Incremental Cost-Effectiveness Ratio (ICER) measured in QALY with a maximum threshold of £30,000/QALY*
	• Cost effectiveness • Comparative clinical effectiveness and health-related factors	Incremental Cost-Effectiveness Ratio (ICER) measured in QALY with a presumed threshold of CAD $50,000/QALY
	• Comparative efficacy • Available evidence against appropriate comparator in appropriate "sub-groups"	Additional benefit rating scale Products offering no additional benefit under reference pricing
	• Comparative efficacy • Incremental benefit vs. next best treatment alternative	SMR: Actual benefit ASMR: Improvement in actual benefit over comparator
	• Price of therapeutic alternative and budget impact	Budget impact primarily Cost-effectiveness (Not an official requirement but frequently used in negotiations)

*The £30,000/QALY is the default threshold. There are other appraisal pathways with a higher QALY threshold.

Courtesy: Apperture LLC, for the source slide please contact ambi@apperturehealth.com

HTA Evolution in the US: Artifact of Fragmented Healthcare System

Source: https://healthpolicy.usc.edu/research/health technology-assessment-for-the-u-s-healthcare-system/

Things are changing in the US with the implementation of the IRA. It's impact on the HTA implementation will become clear in near future. Key difference from Europe is that HTA evaluation are conducted in the beginning in EU at the time of drug launch. In the US, CMS may implement HTA process 9/13 years in drugs' patent life based on whether it is small/big molecule.

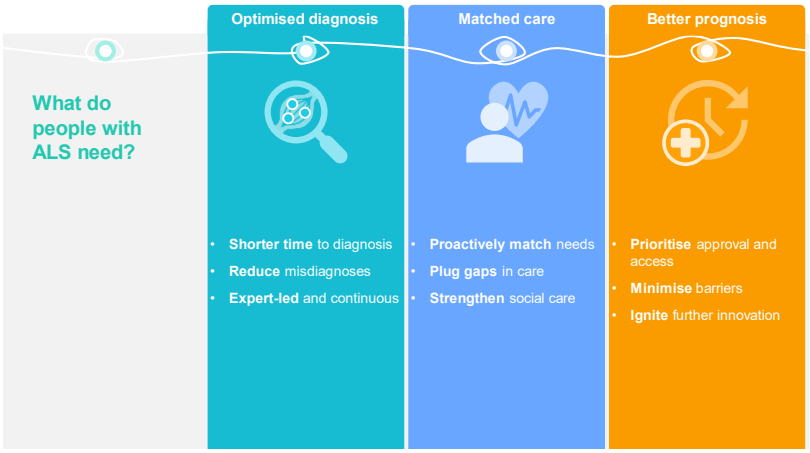
Source: https://avalere.com/videos/howlife-sciences-organizations-can-plan-for-ira-policy-changes

*Slides by Hemant Phatak

Calaneet Balas of the ALS Association in the U.S. addressed the significant disparities in access to ALS/MND treatments globally, using an example from the Philippines where limited access to Riluzole is a major challenge due to its high cost and scarcity. The lack of clinical trials, epidemiological studies, and government support, further exacerbates the situation in the Philippines.

In the U.S., there are ongoing concerns about reimbursement challenges, especially given the recent case involving an Alzheimer's drug, where CMS chose not to cover an FDA-approved drug, raising concerns about impact on other therapeutic areas. There is also an alarming emerging trend of using clinical trial design as a weapon to restrict access, where payers use inclusion criteria as reasons for denying coverage. This creates a significant barrier to access, requiring ongoing vigilance and advocacy by the ALS/MND community. In the U.S. there is also an effort underway to ban the use of quality-adjusted life years (QALYs) to determine value for new therapies, as it poses another access barrier.

Evy Reviers of EUPALS and ALS Liga in Belgium, and **Julian Großkreutz** of EUPALS and the University of Lubeck in Germany described policy recommendations from the ALS EU Coalition, which comprises various participants, including national allies, scientific experts, industry partners, and members of the European Parliament. The coalition's focus is divided into three main topics: optimizing diagnosis, matching care proactively, and better prognosis. Specific emphasis is placed on the "better prognosis" topic, which aims to prioritize approval and access, minimize barriers, and encourage further innovation.



*Slides by Evy Reviers, Julian Großkreutz and EU ALS Coalition

Challenges in Europe related to ALS/MND research and development include the need to increase awareness of accessibility to clinical trials. Europe faces difficulties due to the complexity of rare diseases like ALS/MND, and alignment is needed between researchers, clinical experts, medicine developers, regulatory bodies, and payers to improve clinical trial design. There is an urgent need to expedite access decisions and reduce unnecessary delays for people living with ALS/MND. One important step forward would be to harmonize global standards for ALS/MND decisions on new treatments, ensuring the inclusion of patient evidence, opinions, and reported outcomes in the decision-making process. Another recommendation is to fast-track approvals and provide for conditional approvals across Europe. Additionally, there is a need to capture wider impacts of new medicines, beyond survival rates, to assess the holistic value of treatments.

Group Discussions

Roundtable participants participated in two small group discussions to debrief on the expert presentations and provide specific insights about their geographies' access experiences and challenges. Each participant was invited to share the top 1-2 challenges their regions face, as well as their top solution "if they could wave a magic wand."

Regulatory:

Challenge: Discrepancies in regulatory processes and approvals across different countries.
Solution: Advocate for global regulatory harmonization to streamline approval pathways.

Challenge: Lengthy approval processes, especially in Spain, for clinical trials and commercialization.
Solution: Streamline processes across countries and enhance clinical trial design for efficiency.

Challenge: Delays in treatment availability even after approval.
Solution: Propose conditional approvals based on other countries' approvals/establish regulatory floors.

Challenge: Frustration with regulatory bureaucracy.
Solution: Advocate for faster approval processes and global harmonization of regulatory standards.

Challenge: Duplication of efforts among regulatory bodies and reimbursement agencies in Canada.
Solution: Improve coordination and communication among regulatory entities.

Challenge: Differences in regulatory standards.
Solution: Advocate for global regulatory harmonization for more efficient drug approvals.

Challenge: Ensuring global manufacturing and supply chain capabilities.
Solution: Address both regulatory approvals and supply chain stability for global access.

HTA Access and Coverage/Payor Issues:

Challenge: Challenges related to Health Technology Assessment (HTA) access and varied price settings.
Solution: Call for a single HTA body for Europe and efforts to establish a clear standard.

Challenge: Payers using clinical trial criteria to limit access to approved therapies.
Solution: Engage/educate primary care physicians for early disease recognition, more access to trials.

Challenge: Inadequacies in reimbursement routes in the UK for rare diseases like MND.
Solution: Advocate for more flexible approach to assess rare diseases in publicly funded health systems.

Challenge: ALS/MND patients facing challenges with cost-effectiveness metrics like QALY.
Solution: Advocate for fair assessments considering functional disabilities and patient needs.

Challenge: Prohibitive drug costs and absence of generics in South Africa.
Solution: Address disparities in access and affordability through regulatory intervention.

Challenge: Limited access due to high treatment costs.
Solution: Highlight national initiatives, early access programs, laws addressing unmet medical needs.

Challenge: Payors requiring “fail first” for SOD1 patients.
Solution: Advance policy change to support biomarker-directed therapies in front line setting.

Challenge: Differences among Health Technology Assessment (HTA) bodies.
Solution: Advocate for harmonization and clear standards to navigate varied requirements.

Challenge: Cost barriers impacting access
Solution: Collaborate within the ALS/MND community / with other diseases to address common challenges.

Access to Clinical Trials:

Challenge: Limited access to clinical trials, especially for those in rural areas.
Solution: Embrace telemedicine to include remote participants, improving accessibility.

Challenge: Breakdown in the population representation in clinical trials.
Solution: Reshape assessment methods for biology and functional deficits for more inclusive trial results.

Challenge: Limited global data on ALS/MND progression, biomarkers, and patient outcomes.
Solution: Advocate for global efforts to collect comprehensive data for more representative trials.

Early Diagnosis:

Challenge: Importance of early diagnosis and streamlined access to trials.
Solution: Improve education for healthcare professionals for early symptom recognition.

Challenge: Difficulty in early diagnosis.
Solution: Emphasize the importance of early diagnosis and education for healthcare professionals.

Challenge: Difficulty in diagnostic tools approval.
Solution: Advocate for easier approval processes for diagnostic tools.

Patient-Centric Approach:

Challenge: Incomplete consideration of the patient journey.
Solution: Adopt a patient-centric approach, considering the entire ALS/MND patient journey.

Challenge: Limited discussion on caregivers.
Solution: Acknowledge the role of caregivers and consider their needs in access discussions.

Communication and Information:

Challenge: Lack of clear communication on ALS/MND.
Solution: Work towards a universal language on ALS/MND to bridge communication gaps.

Challenge: Gap in access to information.
Solution: Work towards universal access to information on trials and genetics.

Challenge: lack of easy national guidelines on genetic testing and counseling.
Solution: Develop clear national guidelines and make basic information universally accessible.

Next Steps

The Alliance's Advocacy and Public Policy Advisory Council will review the meeting summary and, given the wealth of ideas and feedback from the group discussions, will prioritize next steps to support global efforts to enhance access to treatment for all people living with ALS/MND. Future Roundtable meetings will address other elements of the Fundamental Rights.