Improving Basic Research, Clinical Trial Infrastructure, and Community Engagement to Support Drug Development for ALS

Day 1 – Wednesday, January 27th

Virtual Private Workshop — January 27 & January 28, 2021

Duke | MARGOLIS CENTER *for* Health Policy

Welcome & Introduction

Mark McClellan, MD, PhD

Director, Duke-Margolis Center for Health Policy

Remote Participation Instructions

- Mute & Slides
- **You have been placed on mute**; speakers can mute/unmute throughout
- We will advance the slide deck, please prompt us to advance

- Meeting Information
- Meeting materials will be distributed after the meeting & are available on the calendar invite

- Questions & Comments
- Please go on video and use the "raise hand" Zoom option if you'd like to speak, we'll pass the microphone and you can unmute
- Please feel free to type your question into the Zoom group chat or use the raise hand function
- Zoom Issues? Please Zoom message Sarah Sheehan or email sarah.sheehan@duke.edu

Meeting Agenda | Day 1

Fireside Chat: Perspectives from FDA Leadership

- Discuss challenges impeding therapeutic advancement and key lessons learned from clinical development and review
- Discuss ongoing efforts to support ALS research and therapeutic development
- Discuss approaches to addressing key challenges and strengthening the ALS drug development pipeline

Where Are We Now with Drug Development in ALS?

- Highlight the state of the science including basic research, innovative trial design and approaches to data collection

Session 1: Importance and Limitations of Basic and Preclinical Research

- Discuss efforts to address gaps and challenges in disease characterization
- Discuss efforts to increase collaboration and introduce efficiencies in basic and preclinical research
- Discuss efforts to enable the efficient movement of candidate therapies towards clinical trials

Session 2: Considerations for Innovative Trial Designs

- Discuss the potential of innovative trial designs to support more efficient evidence generation
- Discuss scientific and practical considerations for the conduct of trials with innovative designs

Meeting Agenda | Day 2

Session 3: Research Infrastructure and Data Sharing for ALS

- Discuss how the enhancement of a shared data infrastructure can support disease characterization, biomarker development, and the capture, efficient use and reuse of clinical data
- Discuss approaches for improving the utility and interoperability of shared data resources

Session 4: Understanding What is Meaningful for Patients - Recruitment, Patient Experience Data, and Expanded Access

- Discuss how to meaningfully incorporate patients' experiences, perspectives and priorities into clinical trials
- Discuss approaches for increasing access to clinical trials and decreasing participant attrition

Session 5: Coordination, Collaboration, and Shared Strategy

- Discuss next steps and stakeholder roles to support ALS research and therapeutic development
- Discuss feasible approaches to improving the quality and availability of tools to support disease characterization
- Discuss next steps for maximizing the utility of innovative approaches to trial design

Fireside Chat: Perspectives from FDA Leadership

12:05pm – 12:30pm

Where are We Now with Drug Development in ALS?

Jinsy Andrews, MD, MSc, FAAN

Associate Professor of Neurology, Director of Neuromuscular Clinical Trials

Columbia University

WHERE ARE WE NOW WITH DRUG DEVELOPMENT IN ALS?

Jinsy Andrews, MD, MSc, FAAN
Director of Neuromuscular Clinical Trials,
Investigator, Motor Neuron Center,
Associate Professor of Neurology
Columbia University Irving Medical Center, NY, NY

Basic Research, Clinical Trial Infrastructure, and Community Engagement to Support Drug Development for ALS

Duke Margolis Center for Health Policy

January 27 & 28, 2021

Disclosures

- Served as on the DSMB for AL-S Pharma
- Serve as a consultant for Avexis, Biogen, Cytokinetics, Denali and Wave Therapeutics
- Receive research funding from Orion Pharma, Biogen, Novartis, Roche, Project ALS and the Healey Foundation
- Serve as NEALS Consortium Co-Chair, Board of Trustee Member for the National ALS Association , and serve on the Scientific Advisory Committee to the Healey Center at MGH

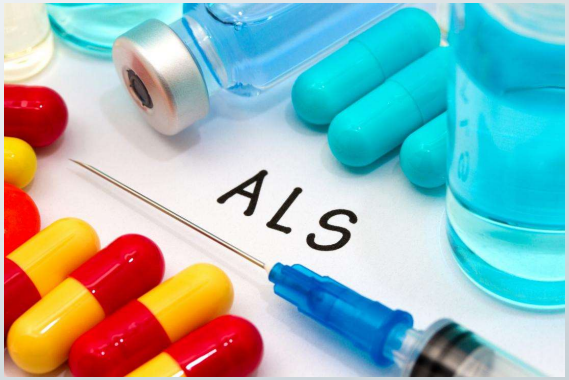
Objectives

- Discuss current ALS treatment landscape
- Review the clinical trial pipeline in the Unites States
- Highlight recent clinical trial results
- Innovations and collaborations in ALS clinical research
- Impact of increasing knowledge of genetics in ALS

Why are we here?

There has been exponential growth in scientific knowledge in ALS

https://pubmed.ncbi.nlm.nih.gov/?term=Amyotrophic+Lateral+Sclerosis&sort=date



https://www.medicalnewstoday.com/articles/321900

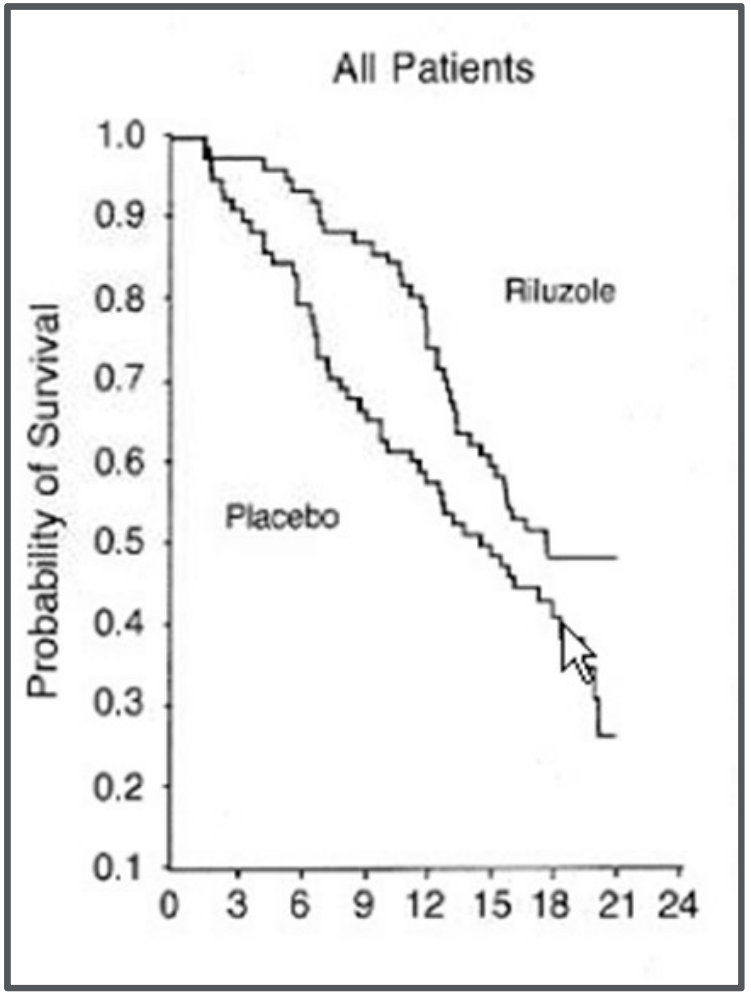
CURRENT TREATMENT OPTIONS FOR ALS

Riluzole
Edaravone

Current Treatment Landscape: Riluzole

- First of 2 trials was a randomized, double-blind, clinical study conducted in France/Belgium for 13 to 18 months
- 155 patients randomized to either 50 mg of riluzole twice daily v. placebo
- Statistically significant effect on the rate of survival (defined as time until tracheostomy or death)
- Benefit was on average 90 days longer in the riluzole-treated group than in the placebo-treated group

The survival advantage at the end of the placebo-controlled period:
37 % [29 of 78] placebo vs.
49 % [38 of 77] with riluzole
(P = 0.046)



Bensimon, et al. *N Engl J Med* 1994; 330:585-591

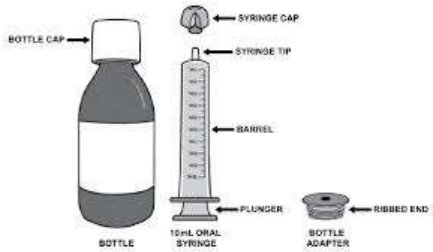
Current Treatment Landscape: Riluzole

Oral tablet was approved for the treatment of ALS in early 1995

- Showed modest benefit based on two controlled clinical trials
- Dosing: 50 mg twice daily

Oral liquid form of riluzole

- Thickened liquid formulation (5mg/ml = 50 mg) administered twice daily via oral syringe
- Received approval in September 2018



Oral film of riluzole

- Received approval November 2109
- Dosing 50 mg twice daily

https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/020599s011s012lbl.pdf

Current Treatment Landscape: Edaravone

- Study conducted in Japan between 2011 to 2014
- 137 patients that completed the observation period were randomized:
  Edaravone (n= 69)
  Placebo (n=68)
- Primary outcome: **Change in ALSFRS-R**
- Edaravone: −5.01 (SE 0.64)
- Placebo: −7.50 (SE 0.66)
- LSM difference = **2.49** (SE 0.76, 95% CI 0.99–3.98; p=0.0013)

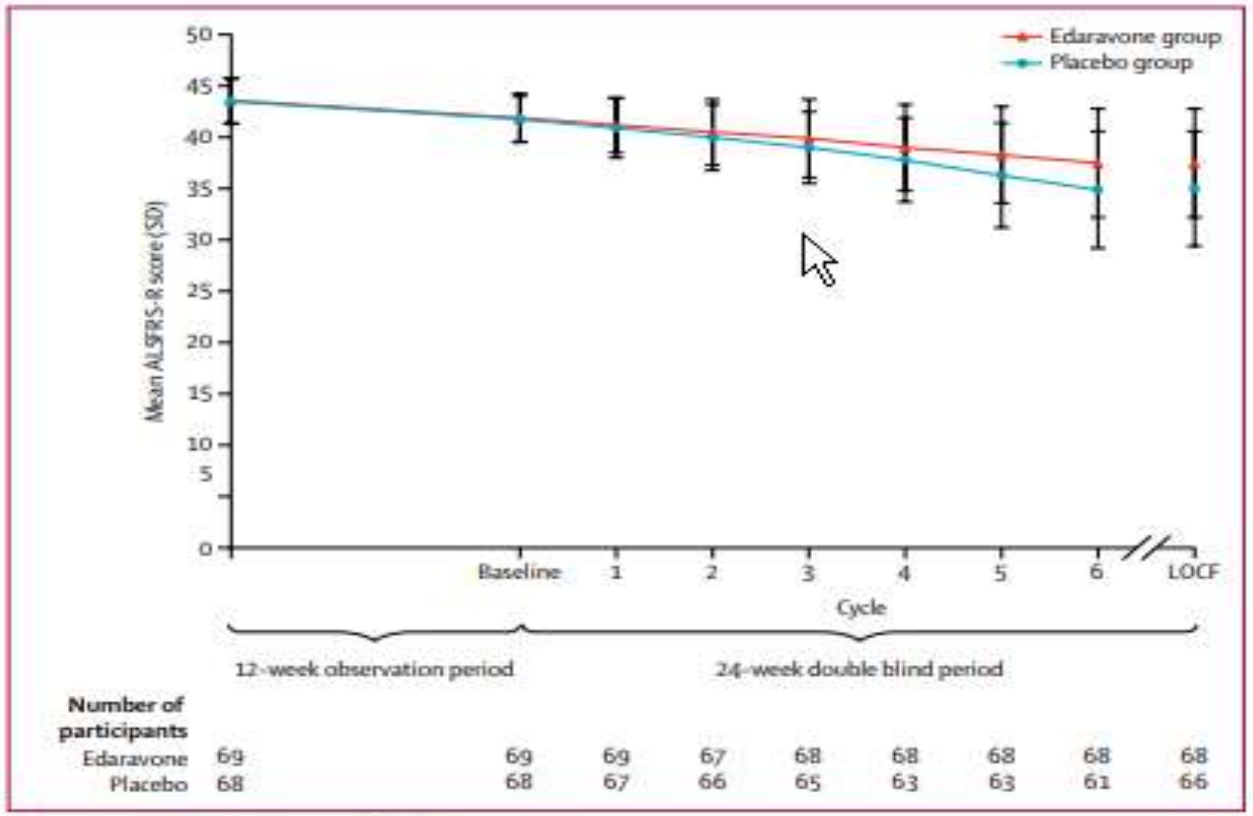


Figure 2: Mean ALSFRS-R scores during treatment
For patients with missing values at the end of cycle 6, data were imputed by the LOCF method, provided that they had completed at least cycle 3. ALS=amyotrophic lateral sclerosis. ALSFRS-R=Revised ALS Functional Rating Scale. LOCF=last observation carried forward. One patient's evaluation at the end of cycle 2 was excluded from analysis as the clinician assessing ALSFRS-R score did not have adequate training.

Writing Group. *Lancet Neurol.* 2017 Jul;16(7):505-512.

Current Treatment Landscape: Edaravone

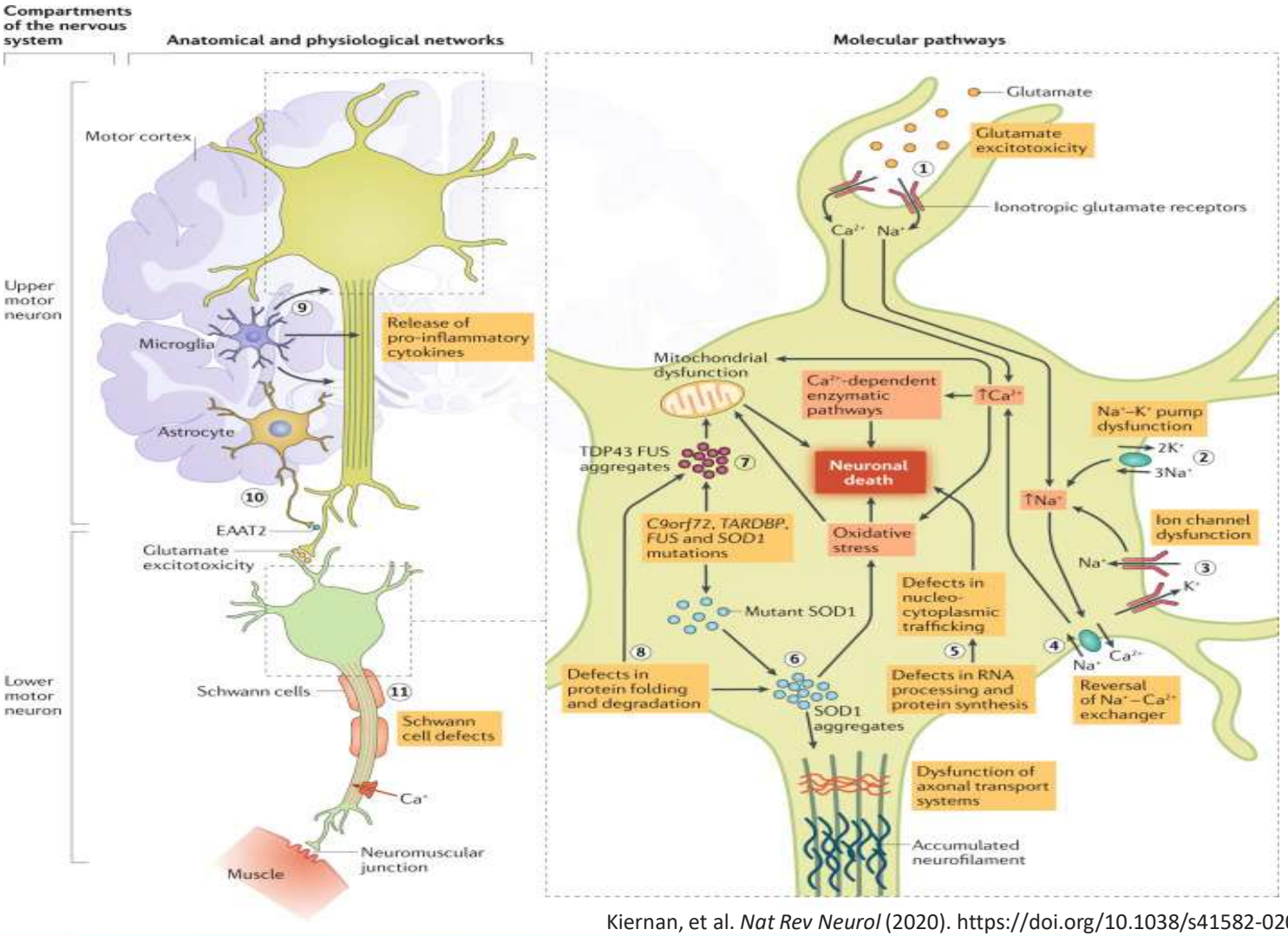
Edaravone was approved for ALS in 2017

Administered intravenously 60 mg over 60 min

- Once a day IV dosing
- One cycle of treatment for 28 days
  - 1st cycle: 14 day administration & 14 days cessation
  - 2nd cycle or after: 10 of 14 day administration & 14 days cessation

Therapeutic Approaches for ALS

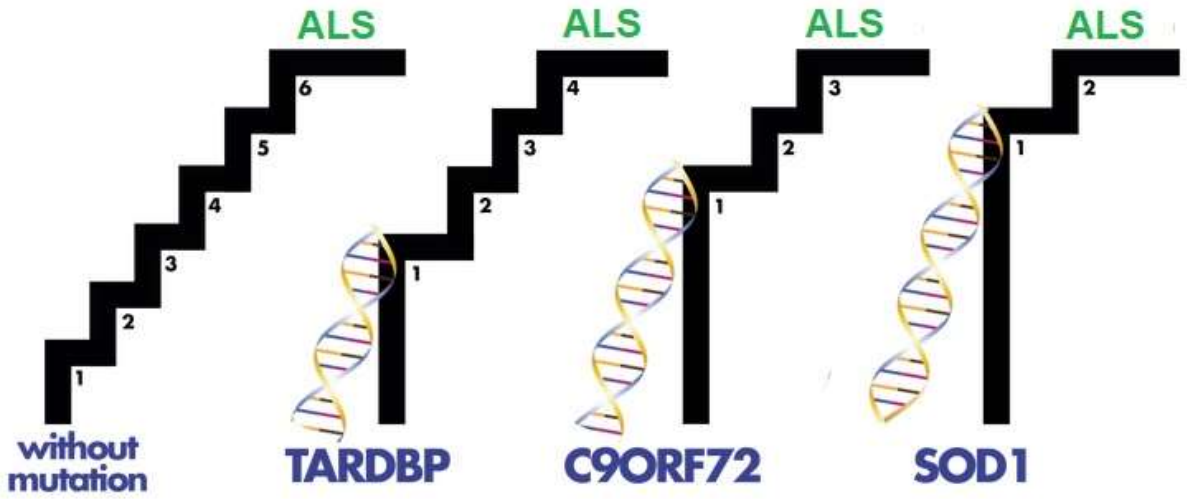
- **Targeting specific gene mutations in ALS**
- **Inhibit specific mechanisms associated with motor neuron degeneration**
  - e.g.: Glutamate excitotoxicity, Oxidative stress, mitochondrial dysfunction, endoplasmic reticulum stress, complement inhibition, heat-shock protein inducing, kinase inhibition
- **Improving nerve and muscle communication**
- **Improving the muscle response to diminished nerve input**
- **Stem cells approaches**
  - Regeneration/neuroprotection of nerve cells (direct injection)
  - Delivering protective factors to the motor neurons (MSC)
  - Improving the support cells surrounding the motor neurons (glial cells)



Kiernan, et al. *Nat Rev Neurol* (2020). https://doi.org/10.1038/s41582-020-00434-z

Evolving theory of how ALS happens

- **The six steps theory**
  Using a mathematical model, previously used by cancer researchers, Al-Chalabi and colleagues (2014) suggested that it takes six steps to trigger ALS. The number of steps might be different (and likely reduced) in ALS caused by specific genes. Each step represents a separate event that could be a genetic, environmental or lifestyle factor with the last one



Al Chalabi et al. *Lancet Neurol.* 2014 Nov 13; 13(11): 1108–1113

CURRENT ALS CLINICAL TRIAL LANDSCAPE

Active clinical trials in the United States

ALS Clinical Trial Pipeline (United States)

Phase 1
GDC 0134+
AT 1501 (anti-CD40L)
Darunavir, ritonavir, dolutegravir, TAF (HERV-K suppression)*
Perampanel*
BIIB100*
BLZ945*

Phase 2
ANX005
ALZT-OP1a*
AT-1501
Clenbuterol+
Cipro/Celecoxib+
Fingolimod
Inosine+
L-serine*
Memantine*
Pegcetacoplan*
Ranolazine*
Retigabine
RNS60+
Tocilizumab
Theracurmin*
L-serine*

PLATFORM TRIAL
• Zilucoplan • Verdiperstat • CNM-Au8 • Pridopidine

Phase 3
Arimoclomol+
Edaravone (oral)*
Ravulizumab*
Ibudilast *
Masitinib*
Reldesemtiv

Approved Therapies
Riluzole
Edaravone
Nuedexta (PBA)

ALS Clinical Trial Pipeline (United States)

Cell Therapies
T regs and IL2* *(Lymphocytes)+*
NurOwn™*(Modified MSC)+*
Q cell *(human glial progenitor)*
CNS10-NPC-GDNF
Adipose derived MSC *

Gene Directed
SOD1 – Tofersen+
C9orf72 – BIIB078+
C9orf72 – metformin*
Ataxin 2 – BIIB105*
FUS - Jacifusen

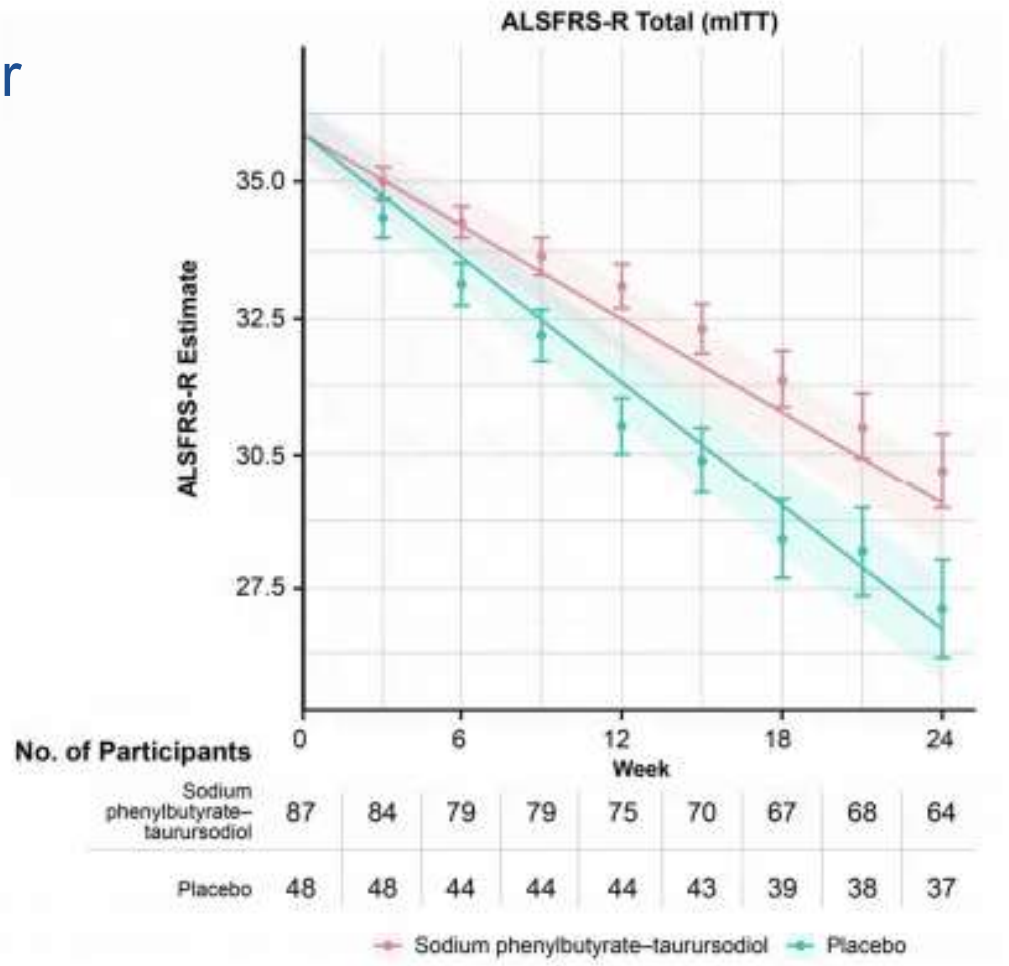
RECENT CLINICAL TRIAL PUBLICATIONS IN ALS

AMX0035 (NEJM 2020, Muscle & Nerve 2020)
Tofersen (NEJM 2020)

AMX0035 (Sodium Phenylbutyrate/Taurursodiol)

Trial of Sodium Phenylbutyrate and Tauroursodiol (AMX0035) for ALS

- 137 patients were randomized to AMX0035 v. placebo
- Mean rate of change in ALSFRS-R score was:
- -1.24 in active
- -1.66 in placebo
- (difference 0.42 pts/month, 95% CI 0.03 to 0.81, p=0.03)
- AE mainly GI; fewer SAE in active arm



Paganoni, et al. *N Engl J Med* 2020; 383:919-930

The clinical trial results for AMX0035 raises some questions for the ALS Community…

Considerations include:

- Rigor of statistical analysis
  - Pre-specified analyses
  - Several previous clinical trial failures in ALS related to carrying forward studies based on post hoc analyses
- Meaning of the endpoints
- Consistency of endpoints

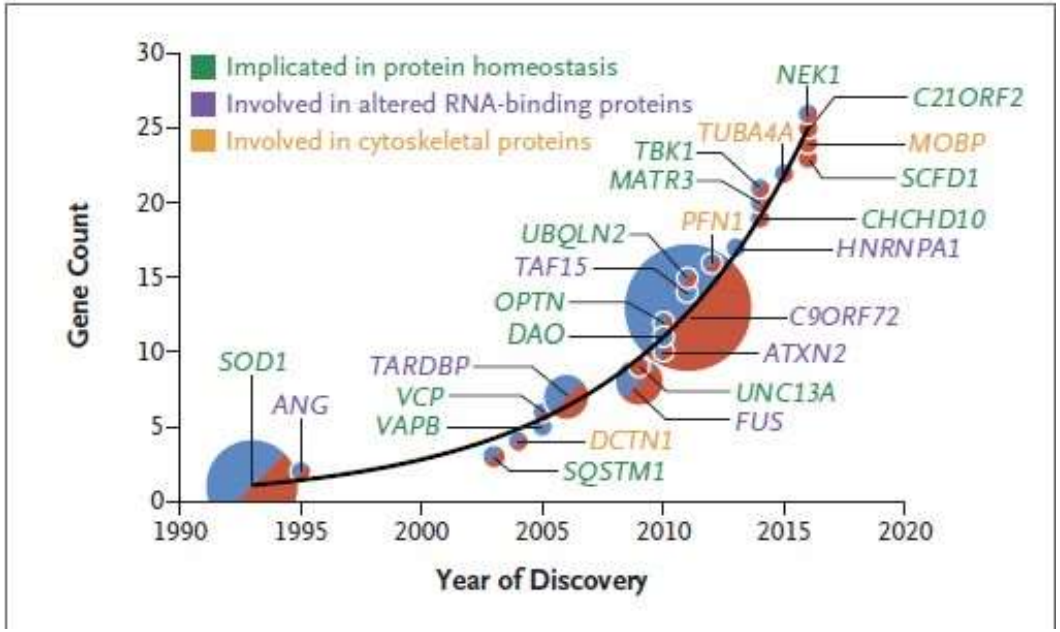
Balance this with:

- Safety and tolerability
- Ease of administration (Frequency and route of administration)
- Potential costs for therapy

GENETICS IN ALS

Complexity of Genetics in ALS

- ALS can result from many possible underlying genetic variations (i.e. different genes can cause ALS)
- Many ALS-associated genes are also implicated in other conditions, including frontotemporal dementia and cerebellar disease
- The distinction between familial and sporadic ALS is not clear-cut, which greatly complicates genetic counselling in ALS



ALS Gene Discovery since 1990. From Robert H. Brown and Ammar Al-Chalabi, *N Engl J Med* 2017;377:162-72

Nature Reviews Neurology 2017; 13**:** 96–104

Tofersen (SOD1 Antisense Oligonucleotide)

The NEW ENGLAND JOURNAL of MEDICINE

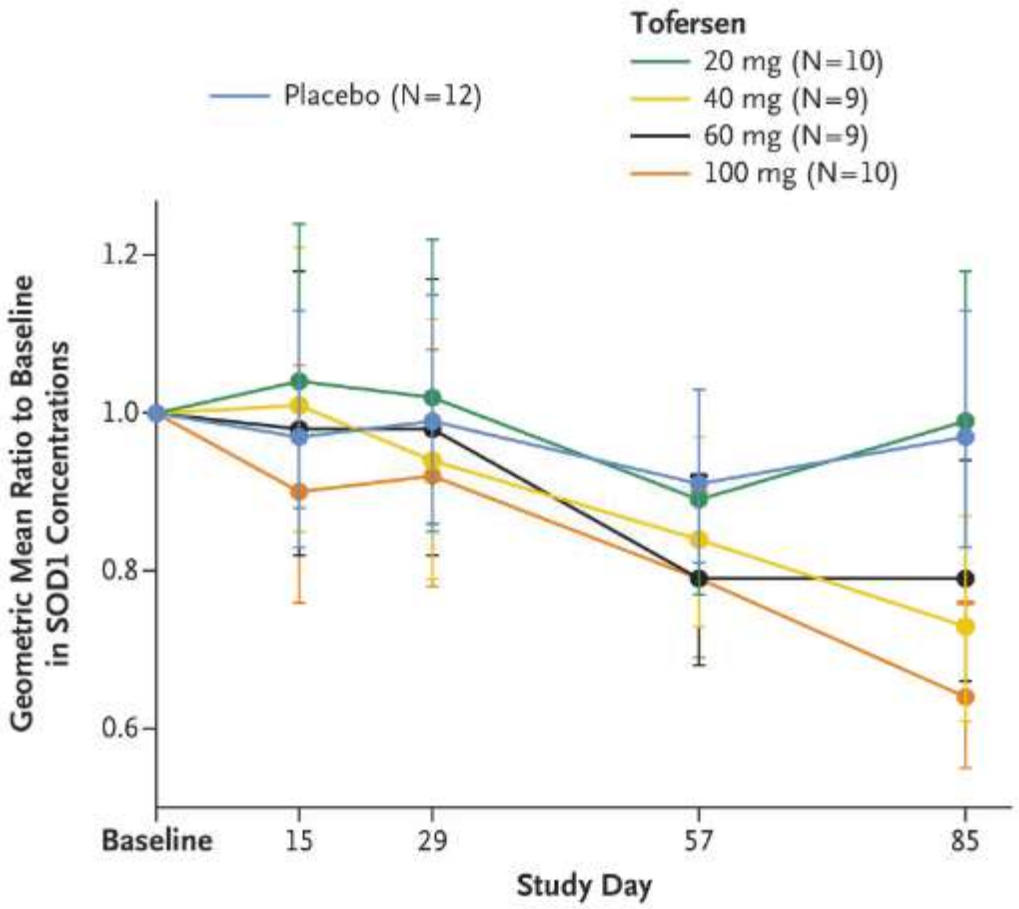
ORIGINAL ARTICLE FREE PREVIEW

Phase 1–2 Trial of Antisense Oligonucleotide Tofersen for *SOD1* ALS

Timothy Miller, M.D., Ph.D., Merit Cudkowicz, M.D., Pamela J. Shaw, M.D., M.B., B.S., Peter M. Andersen, M.D., Ph.D., Nazem Atassi, M.D., M.M.Sc., Robert C. Bucelli, M.D., Ph.D., Angela Genge, M.D., Jonathan Glass, M.D., Shafeeq Ladha, M.D., Albert L. Ludolph, M.D., Nicholas J. Maragakis, M.D., Christopher J. McDermott, M.D., Ph.D., et al.

Phase 1-2 Trial of Antisense Oligonucleotide Tofersen for SOD1 ALS

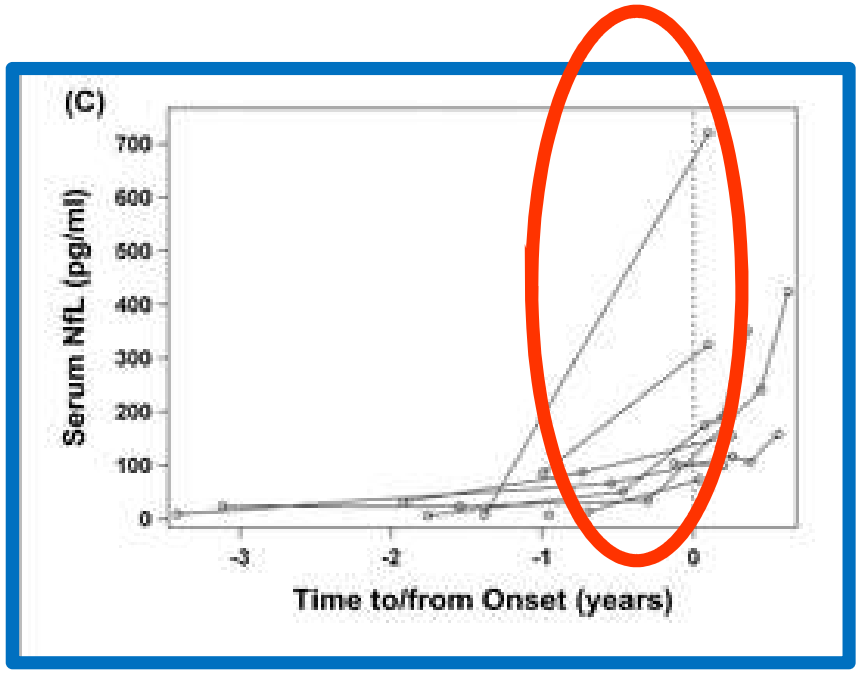
- Phase 1-2 ascending dose trial
- Randomized 3:1
- Primary outcome safety and PK
- Dose dependent decrease of CSF protein



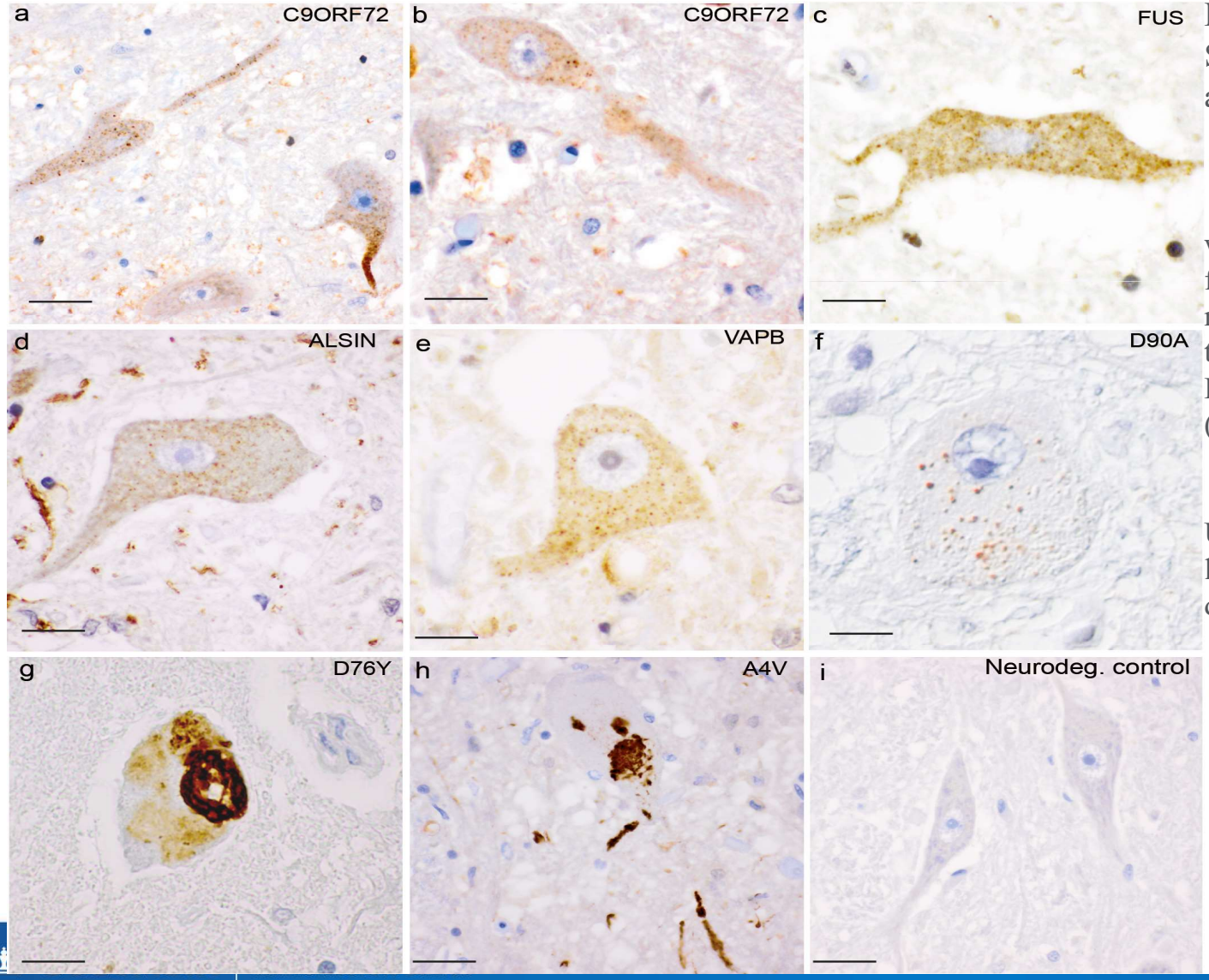
Miller et al, *N Engl J Med* 2020, 383: 109-119

Neurofilament light as a potential biomarker of pre-symptomatic SOD1 ALS and phenoconversion

- The study population: 34 controls, 84 at risk individuals, 10 converters and 17 ALS patients (11 of which had no gene mutation)
- Of the converters all were SOD, except 1 FUS
- Among converters, serum NFL was higher than controls about 12 months prior to any symptoms or signs of disease



Benatar, et al. *Annal of Neurol* 2018; 84: 130-139



Morphology of SOD1 aggregates in human autopsies:

wt/wt SOD1:
fine granular aggregates
morphologically very similar to the stable
D90A SOD1
(6 autopsies)

Unstable SOD1 mutants:
larger more
distinct aggregates

Pictures courtesy of
Dr. Thomas Brännström and
Dr. Karin Forsberg
Umeå University, Sweden

Forsberg, et al. *J Neurol Neurosurg Psychiatry* 2019

Rapid increase in genetic understanding in ALS and availability of technology to target gene mutations has an impact….

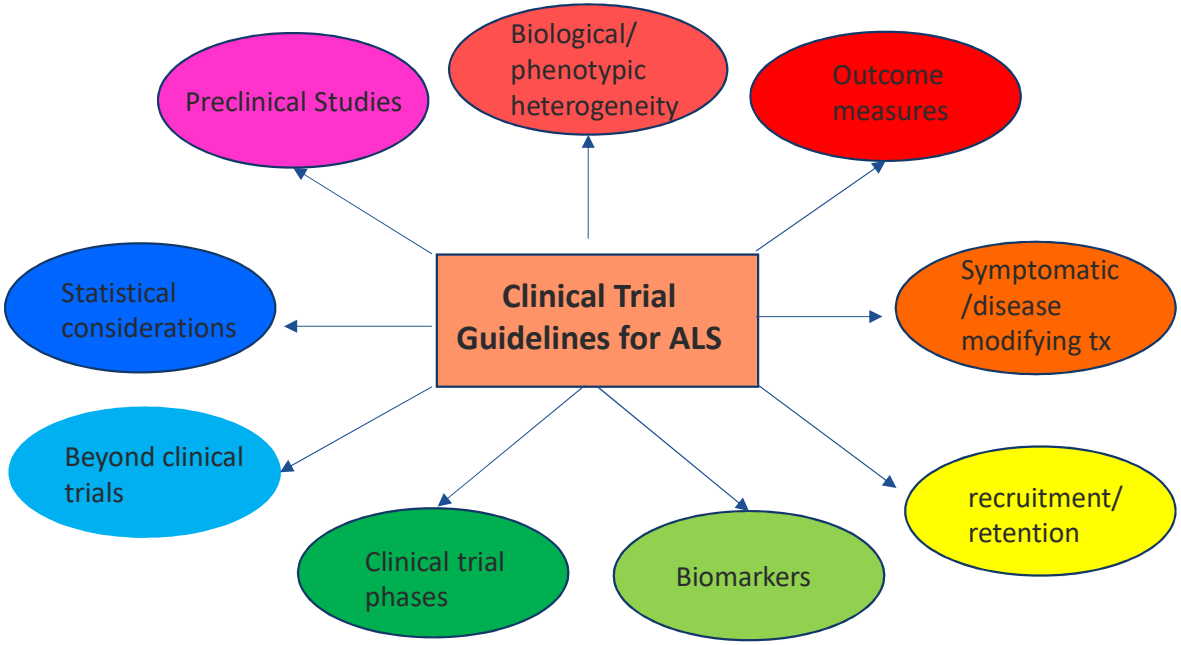
- Trial design needs to be carefully considered when developing investigational drug targeting specific gene
- Need to understand genotype/phenotype correlation in subpopulations/ natural history
- Drug development pipeline may also enable targeting pre-symptomatic carriers or other subpopulations
- Clinical practice implications
  - Reducing time to diagnosis
  - Genetic testing
  - Genetic counseling
  - Observational studies to study symptomatic and pre-symptomatic cohort

EVOLVING DRUG DEVELOPMENT LANDSCAPE

Amyotrophic Lateral Sclerosis

Evolving Drug Development Landscape

A consensus committee comprising 140 key members of the international ALS community (ALS researchers, clinicians, patient representatives, research funding representatives, industry, and regulatory agencies)



Evolving Drug Development Landscape

- 112 guidelines and their associated backgrounds and rationales were published
- The group prioritized 15 guidelines with the greatest potential to improve ALS clinical research
- The revised Airlie House ALS Clinical Trials Consensus Guidelines serve to help improve clinical trial design and accelerate the development of effective treatments for patients with ALS

van den Berg, et al. *Neurology*. 2019 April 09; 92(14).

Evolving Drug Development Landscape

Neurology. 2019 Apr 2; 92(14): e1610–e1623.
doi: 10.1212/WNL.0000000000007242

PMCID: PMC6448453
PMID: 30850440

Revised Airlie House consensus guidelines for design and implementation of ALS clinical trials

Leonard H. van den Berg, MD, PhD,✉ Eric Sorenson, MD, Gary Gronseth, MD, Eric A. Macklin, PhD, Jinsy Andrews, MD, Robert H. Baloh, MD, PhD, Michael Benatar, MD, PhD, James D. Berry, MD, Adriano Chio, MD, Philippe Corcia, MD, PhD, Angela Genge, MD, Amelie K. Gubitz, PhD, Catherine Lomen-Hoerth, MD, PhD, Christopher J. McDermott, MD, Erik P. Pioro, MD, PhD, Jeffrey Rosenfeld, MD, PhD, Vincenzo Silani, MD, Martin R. Turner, MBBS, PhD, Markus Weber, MD, Benjamin Rix Brooks, MD, Robert G. Miller, MD, Hiroshi Mitsumoto, MD, DSc, and for the Airlie House ALS Clinical Trials Guidelines Group

van den Berg, et al. *Neurology*. 2019 April 09; 92(14).

Evolving Drug Development Landscape

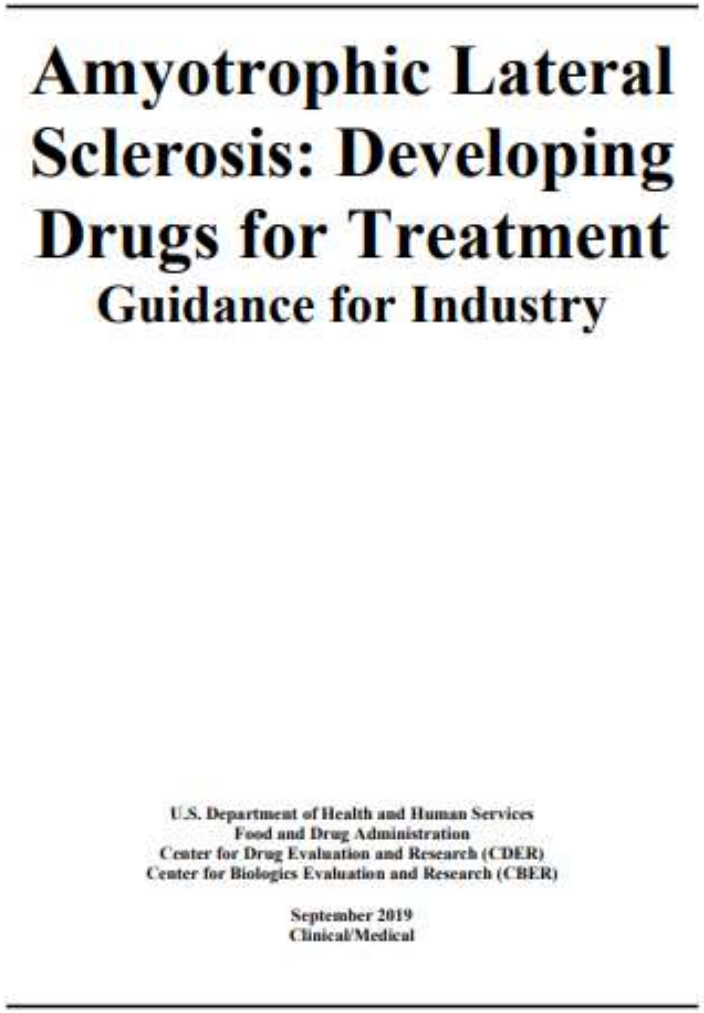
- From 2015 to 2018, there was a multi-stakeholder effort to develop a **Community Guidance** for drug development in ALS

- The Food and Drug Administration (FDA) issued **a FINAL Drug Development Guidance** in 2019 to assist sponsors in the clinical development of drugs for the treatment of ALS

- Specifically, this guidance addresses the FDA's current thinking regarding the clinical development program and clinical trial designs for drugs to support an indication for the treatment of ALS

https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM596718.pdf

Risk/Benefit Considerations:
"When making regulatory decisions about drugs to treat ALS, FDA will consider patient tolerance for risk, and the serious and life-threatening nature of the condition. "



Amyotrophic Lateral Sclerosis: Developing Drugs for Treatment

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

September 2019
Clinical/Medical

https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM596718.pdf

INNOVATION AND COLLABORATIONS IN AMYOTROPHIC LATERAL SCLEROSIS (ALS)

Moving Drug Development Forward for ALS

GTAC

Columbia University College of Physicians and Surgeons | IGM Institute for Genomic Medicine

ALS Association | Biogen

Genomic Translation for ALS Care

- **PI: Matthew Harms, MD** matthew.harms@columbia.edu
- 13 sites in the United State and Scotland
- 1028 subjects enrolled (~1.5 new patients daily)
  - Longitudinal outcomes and phenotyping
  - Whole genomes + transcriptomes
  - pBMCs banked for iPSC work
- >900 new genomes analyzed and results returned
- Columbia IGM/GTAC: 6k ALS cases and 60k controls

GTAC Participating Sites

CReATe Consortium

20+ institutional members
- 15 clinical sites

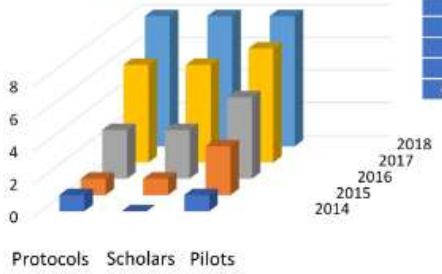
4 PAG (patient advocacy group) partners

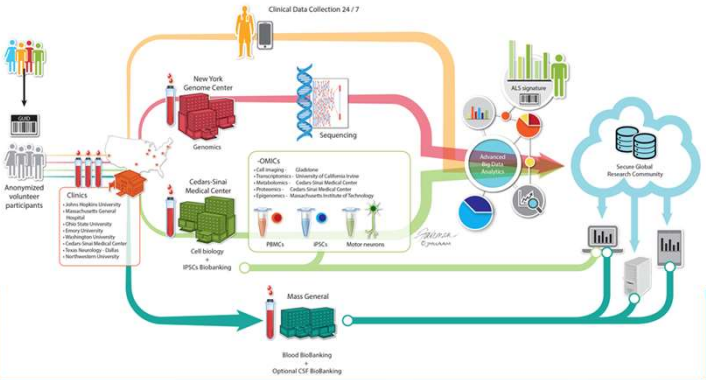
6 other strategic partners

ALS | MDA | SPF | AFTD | Epic | NIH

Protocol #	# Enrolled
8001	719
8002	211
8003	399
8004	47
8005	48
8007	16
8008	364
8009	4
CReATe Connect	1,542

NIH SINGLE IRB MANDATE JANUARY 25, 2018





ANSWER ALS

FISHMAN FAMILY FOUNDATION | alsFINDINGaCURE | American Airlines | Microsoft | NFL | STAY STRONG VS. ALS | ALS ASSOCIATION | PACKARD CENTER | BRUCE EDWARDS FOUNDATION | Google Analytics | BARRY LIPP FOUNDATION | MDA | MGH | JOHNS HOPKINS | IBM WATSON | NEW YORK GENOME CENTER | MIT | CEDARS-SINAI MEDICAL CENTER | GLADSTONE INSTITUTES | Northwestern Medicine | TEXAS NEUROLOGY | WILLIAM H. ADAMS FOUNDATION | accenture | Hartford Foundation | EMORY UNIVERSITY

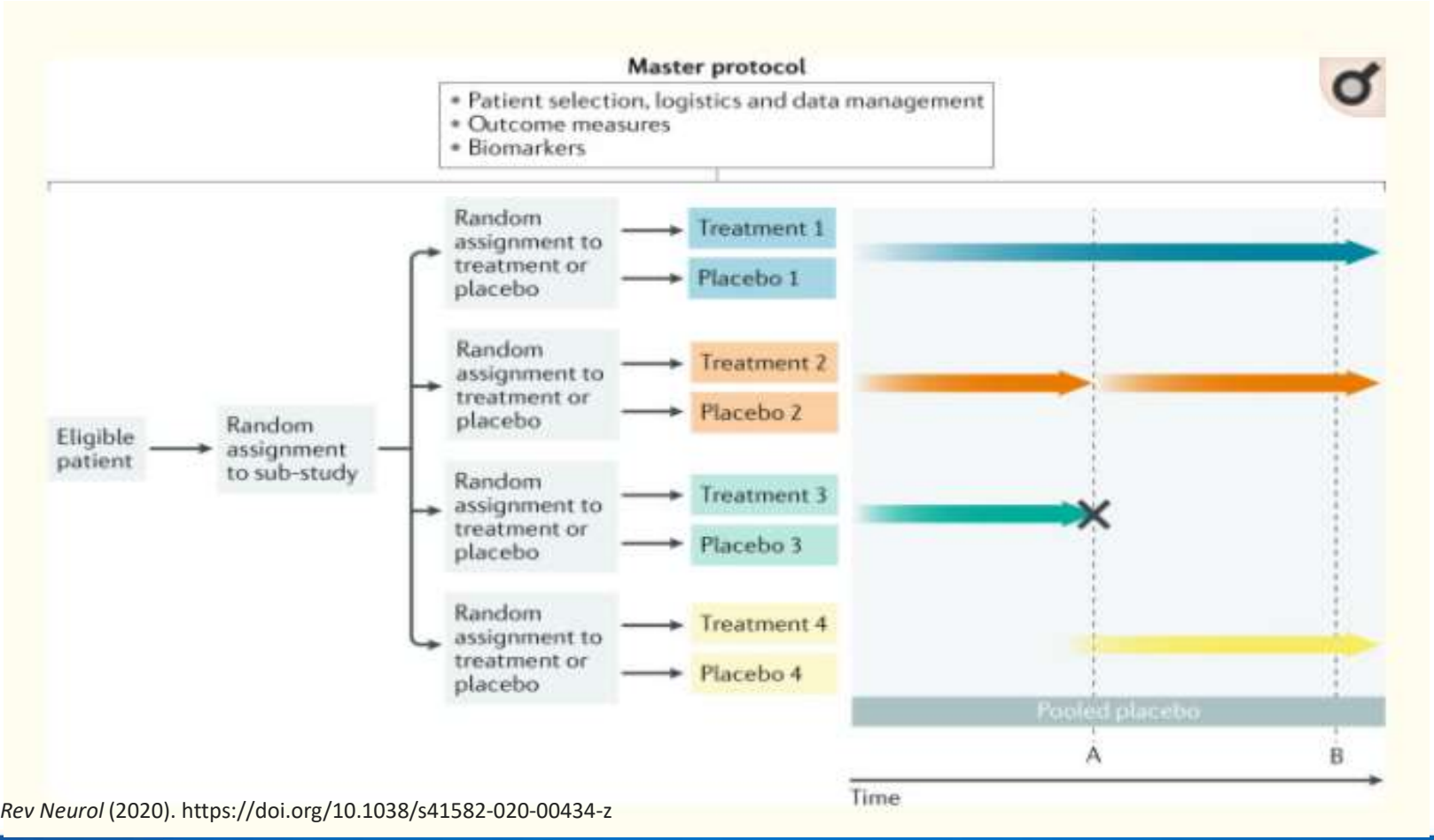
COLUMBIA | COLUMBIA UNIVERSITY IRVING MEDICAL CENTER

Pooled Resource Open-Access ALS Clinical Trials Database

- Over 10,700 fully de-identified clinical patient records
- Placebo and treatment-arm data from 23 Phase II/III clinical trials
- Demographic, lab, medical and family history, and other data elements
- More than 10 million longitudinally collected data points

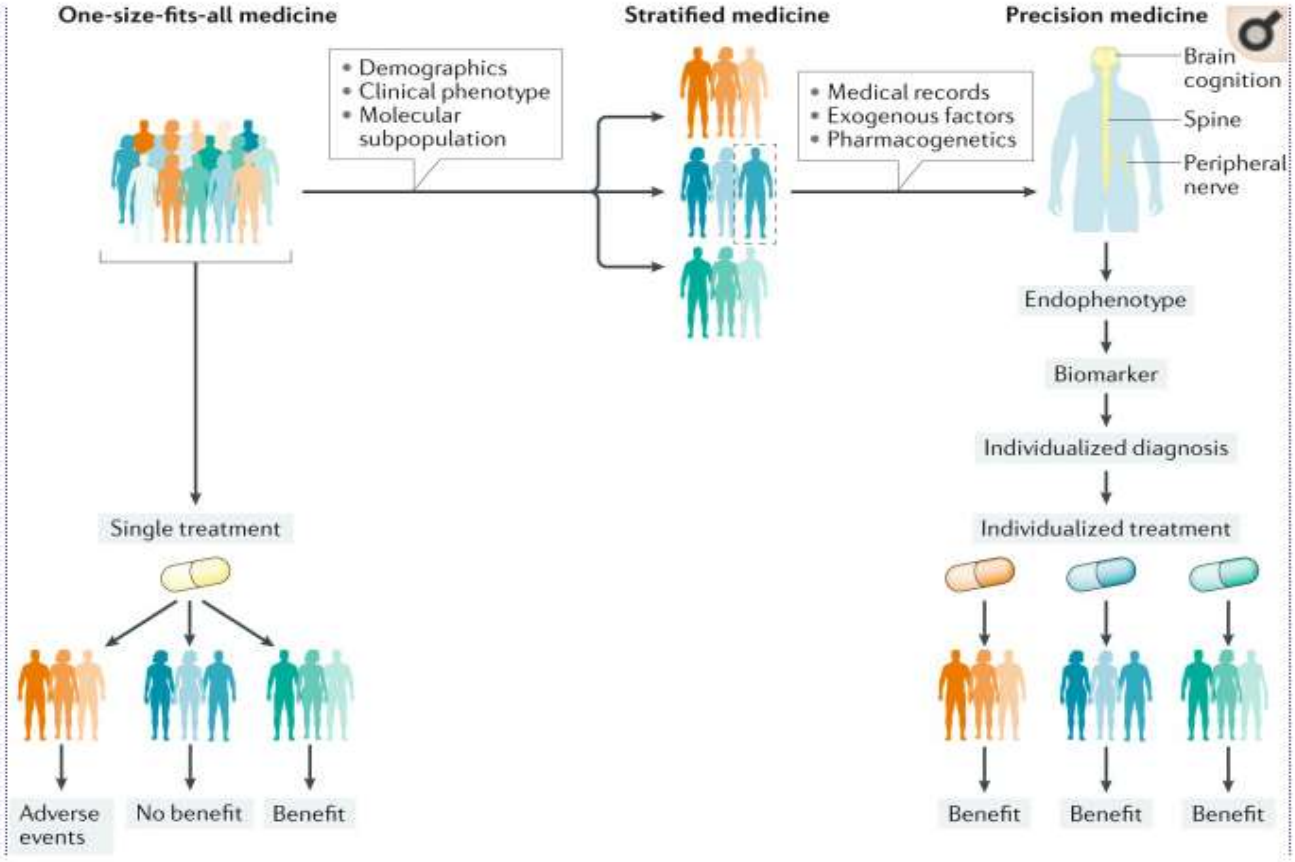
https://nctu.partners.org/ProACT/Home/Index

MASTER PROTOCOL



Kiernan, et al. *Nat Rev Neurol* (2020). https://doi.org/10.1038/s41582-020-00434-z

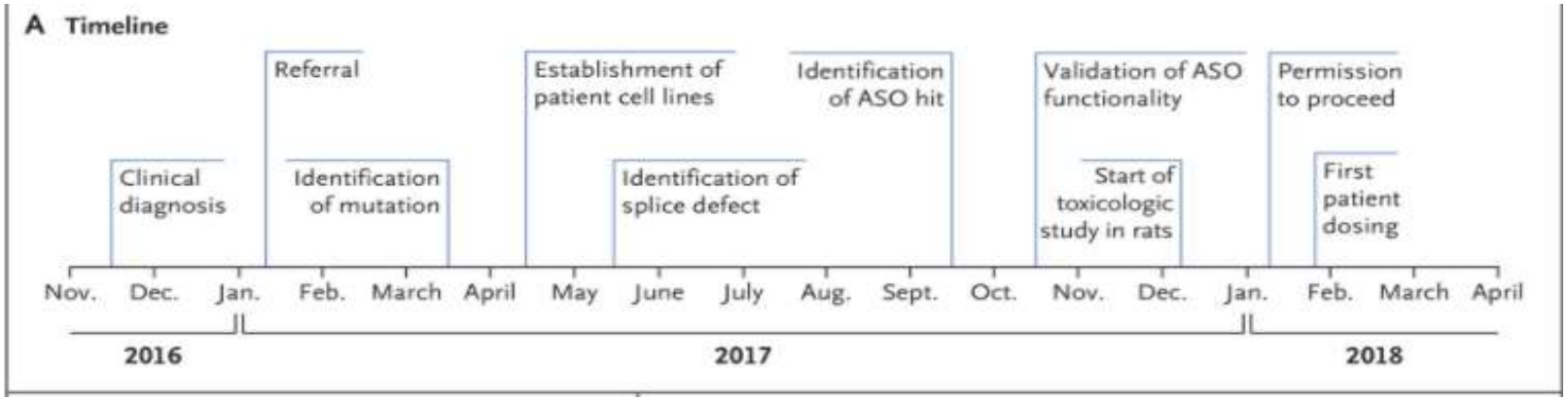
PRECISION MEDICINE APPORACH



Kiernan, et al. *Nat Rev Neurol* (2020). https://doi.org/10.1038/s41582-020-00434-z

“N of 1” / Individualized Therapies

Milasen for Batten’s disease



Jacifusen for first dosing of FUS Associated ALS

- Feb 2019 - Clinical Diagnosis (FUS P525 was identified prior)
- March 2019 - Initiated discussion with collaborators to identify ASO, initiate testing, toxicology and manufacturing
- April 2019 - Initiated regulatory interactions
- May 2019 - Received permission to proceed
- June 2019 - First dose received

PROJECT ALS
FINDING & FUNDING A CURE

THE CORE

IONIS

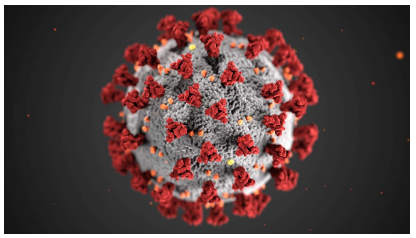
ALS Association

Lingering Questions with Individualized Therapies

- In these situations, What type of evidence is needed before exposing a human to a new drug? Even in rapidly progressing, fatal illnesses?
- what is the minimum assurance of safety that is needed?
- How persuasive should the mechanistic or functional data be?
- How should the dose and regimen be selected?
- How much characterization of the product should be undertaken?
- How should the urgency of the patient's situation or the number of people who could ultimately be treated affect the decision-making process?

Woodcock & Marks, *N Engl J Med* 2019; 381:1678-1680

ALS Clinical Trials In The COVID Era



Primary Goal: to protect participants' safety and to assess the effect of a study drug on ALS progression

Enabled learning how to adjust clinical trial protocols

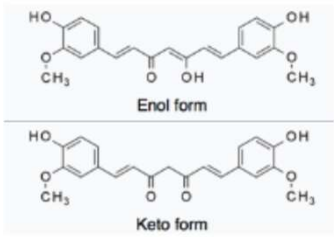
- Virtual visits when in person is not possible
- Local/ home collection of safety assessments (vitals, labs, EKG)
- Maintain study drug supply
- Remote collection of outcome measures (dynamometers, accelerometers, actigraphs and home spirometry)
- Telephone or telemedicine Visits

Andrews, et al. *Muscle Nerve*. (2020) 62:182–6.

Open-label Study of Theracurmin: Piloting a Remote Clinical Trial in ALS

Duke ALS Clinic


Curcumin powder



Courtesy of PI: Dr. Richard Bedlack, Duke University

Concepts for Consideration in Drug Development for ALS

- For life threatening and serious diseases, the concepts that drive drug development
  - **Speed**
  - **Innovation**
  - **Access**
- Other important issues in drug development:
  - Patient voice
  - Data quality
  - Evidence generation
- Are there opportunities for efficiency in drug development?:
  - Expedited pathways with post-approval data
  - Innovative trial design including adaptive pathways and endpoint modification driven by patient focused drug development
  - Use of real-world evidence

Thoughts On Improving Clinical Trial Outcomes for ALS

- Need to focus on understanding the biological processes that trigger the disease and promote disease progression
- Facilitate the translation of genetic and cellular therapies into the clinic
- Develop effective high-throughput screening
- Refinement of clinical biomarkers and integration of biomarker discovery and validation in all trials
- Develop platforms for initial testing in small patient cohorts to identify a biological signal using biomarkers
- Develop patient stratification pathways that better reflect clinical populations
- Increase the use of self-reported patient outcomes
- Widen the use of multi-arm, multi-stage platform trials

Kiernan, et al. *Nat Rev Neurol.* 2020 Dec 18 : 1–15.

Thank You!

Eleanor and Lou Gehrig ALS Center

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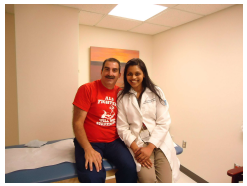
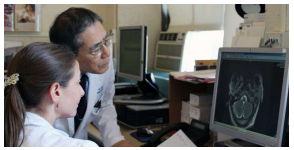
MDA®

ALS Association
Fighting Lou Gehrig's Disease

Project A.L.S.™
FINDING & FUNDING A CURE FOR ALS





Session 1: Importance and Limitations of Basic and Preclinical Research

12:45pm – 1:40pm

Amelie Gubitz

Program Director, Division of Neuroscience

National Institute of Neurological Disorders and Stroke

National Institutes of Health

Erin Fleming

Director of Research Operations

Project ALS

Michael Benatar

Professor of Neurology

Walter Bradley Chair in ALS Research

University of Miami

What are the challenges associated with validating biomarkers, and what approaches may support efficient biomarker validation?

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Benatar, 2021

What are the challenges[2] associated with validating[1] biomarkers, and what approaches[3] may support efficient biomarker validation?

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Biomarker Development

Validation

- Establish proof of concept
- Clinical samples of convenience
- Begin defining context of use

- Pre-analytic considerations
- Assay performance characteristics
- Evaluate impact of potential confounding factors
- Refine context of use

Assay Performance Characteristics
Matrix effects
Assay platform
Analytic sensitivity
Dynamic range
Normal range
Assay reliability
Other: RT stability, freeze-thaw effects, diurnal fluctuation, etc.

* Surrogate marker

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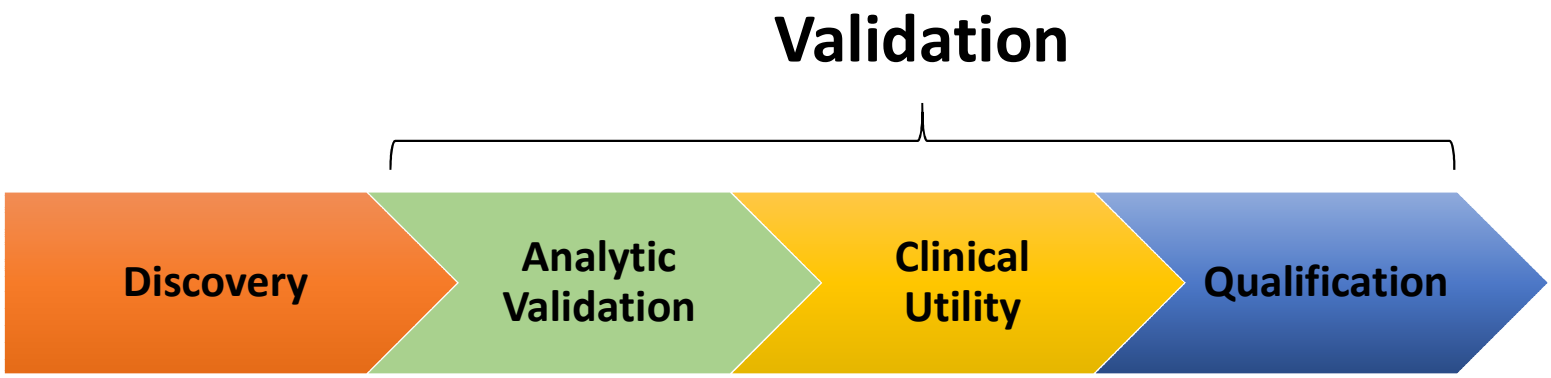
Biomarker Development



- Establish proof of concept
- Clinical samples of convenience
- Begin defining context of use

- Pre-analytic considerations
- Assay performance characteristics
- Evaluate impact of potential confounding factors
- Refine context of use

- Large, carefully-defined clinical cohort
- Well-defined SOPs
- Establish intended clinical use

- Demonstrated clinical utility
- Written context of use
- FDA review for qualification

* Surrogate marker

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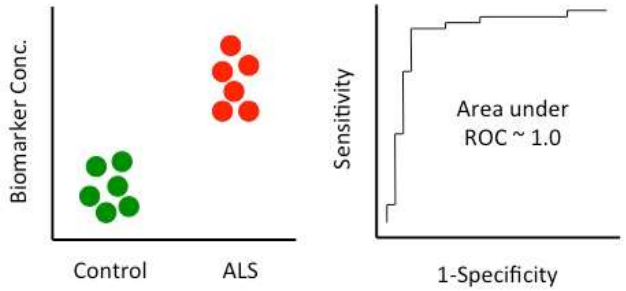
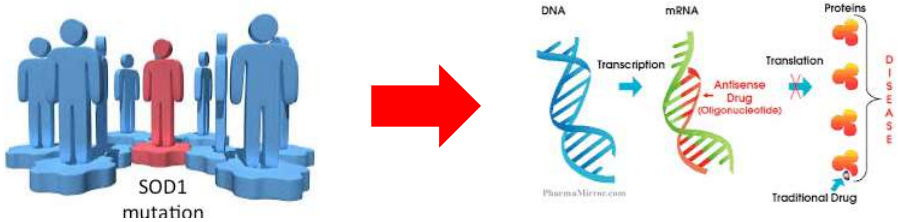
Context of Use

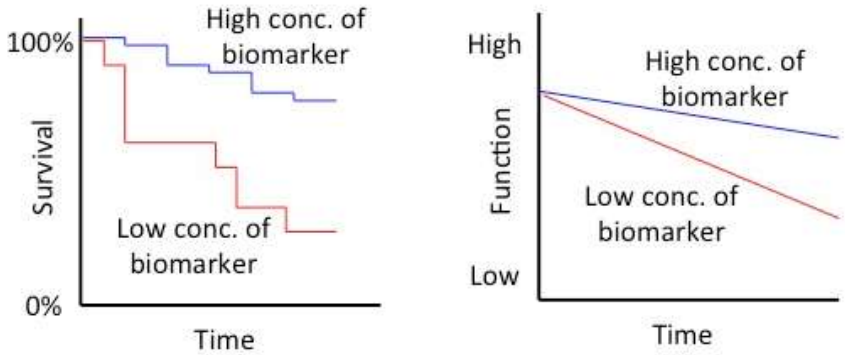
Diagnostic



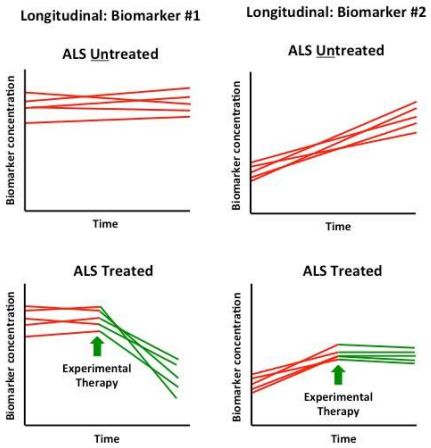
Predictive



Prognostic



Pharmacodynamic



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Approaches

- More nuanced understanding of biomarkers
  - Context-of-use
  - ~~Surrogacy~~
- Close collaboration between discovery scientists and clinician investigators
- Resources: infrastructure, cohorts, funding
- Urgent unmet need: biomarkers of underlying biology

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Lois Freed

Division Director

Division of Pharmacology/Toxicology, Office of Neuroscience

U.S. Food and Drug Administration

Session 1 | Discussion Questions

1. What innovative approaches are being taken to accelerate drug discovery in ALS (e.g., novel ways to identify potential druggable targets) and how can the research community benefit from continued investment in this work?
2. How can the predictive validity of disease models be improved to better support the conduct of clinical trials?
3. What are the challenges associated with validating biomarkers, and what approaches may support efficient biomarker validation?
4. What is the role of pre-competitive collaboration in helping to streamline and accelerate basic and preclinical ALS research?

Session 2: Considerations for Innovative Trial Designs

1:50pm – 2:55pm

Sabrina Paganoni

Co-Director

MGH Neurological Clinical Research Institute

HEALEY ALS Platform Trial

Sabrina Paganoni, MD, PhD

HARVARD MEDICAL SCHOOL

MASSACHUSETTS GENERAL HOSPITAL

Healey Center
Sean M. Healey & AMG Center for ALS at Mass General

NEALS Northeast Amyotrophic Lateral Sclerosis Consortium

NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

BARROW Neurological Institute

Berry Consultants Statistical Innovation

MELIORA

ucb

Ra Pharma

biohaven pharmaceuticals

CLENE NANOMEDICINE

prilenia

SEELOS THERAPEUTICS

TACKLE ALS "DON'T BE SORRY LETS BEAT THIS"

ALS ASSOCIATION

MDA Muscular Dystrophy Association

alsFINDINGaCURE

IAM ALS

ALS ONE

SALSA For a Cure

BASEBALL WINTER MEETINGS

THE ARTHUR M. BLANK FAMILY FOUNDATION

RUN2REVIVE MIND BODY POTENTIAL

“I lost the privilege of working on the human time clock on January 6, 2018

The ALS clock is a lot faster”

Sandy – Person with ALS

Healey Center
Sean M. Healey & AMG Center
for ALS at Mass General

Accelerating innovation for a cure

Merit Cudkowicz, MD, MSc
Sean M. Healey

Traditional Clinical Trial

vs.

HEALEY ALS Platform Trial

Cuts time in 1/2	Cuts costs by 1/3	Reduces placebo

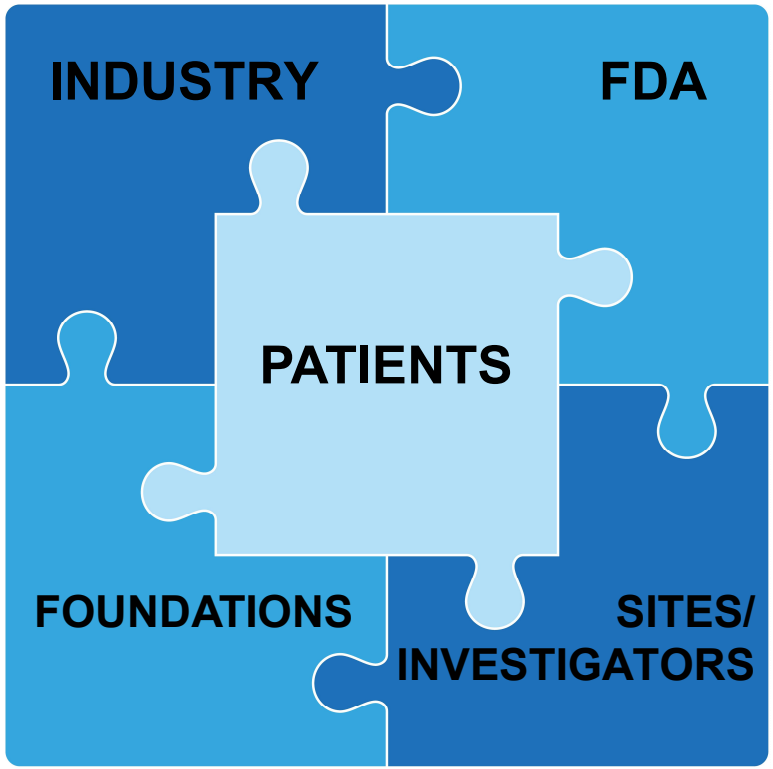
Working with the entire ALS Community to launch the trial rapidly and efficiently

ALS Platform Trial Industry Workshop

"Platform trials may possibly be the best thing I have seen since diagnosis!"

★★★★★

NEALS Northeast Amyotrophic Lateral Sclerosis Consortium



54 TRIAL-READY SITES

1 Central IRB

TRIAL DESIGN COMMITTEE

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Alex Sherman
MGH - Clinical Trial Systems

Hong Yu
MGH - Data Management

Stacey Grabert
MGH - Quality Assurance

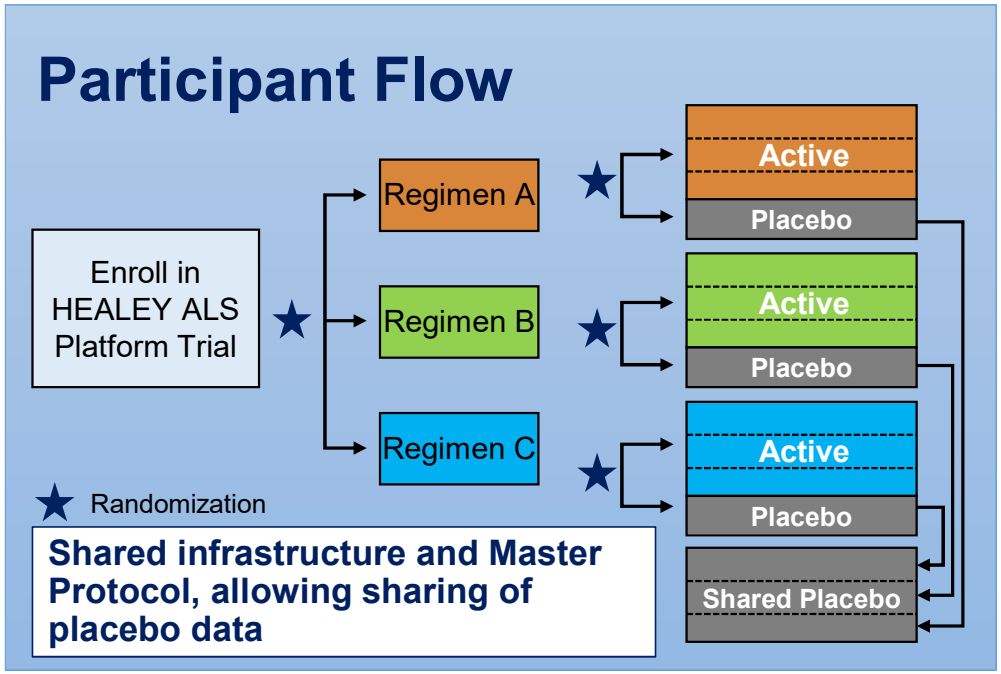
Annette DeMattos
MGH - Grants & Contracts

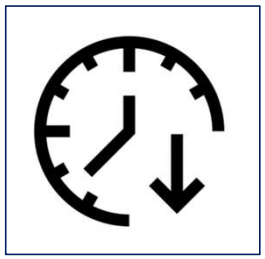
Megan Hall, Rebecca Randall & Gale Kittle
BNI - Monitoring & Outcomes Training

Andrew McGarry, MD & Margherita Torti, MD
Clintrex – Safety Monitoring

Patrick Bolger & Ahmed Fetouh
CMSU – Central Pharmacy

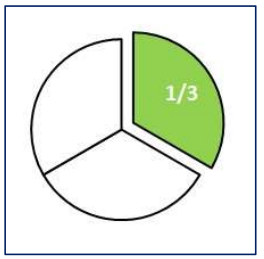
Shared Infrastructure and Master Protocol Allow for Operational and Scientific Efficiencies





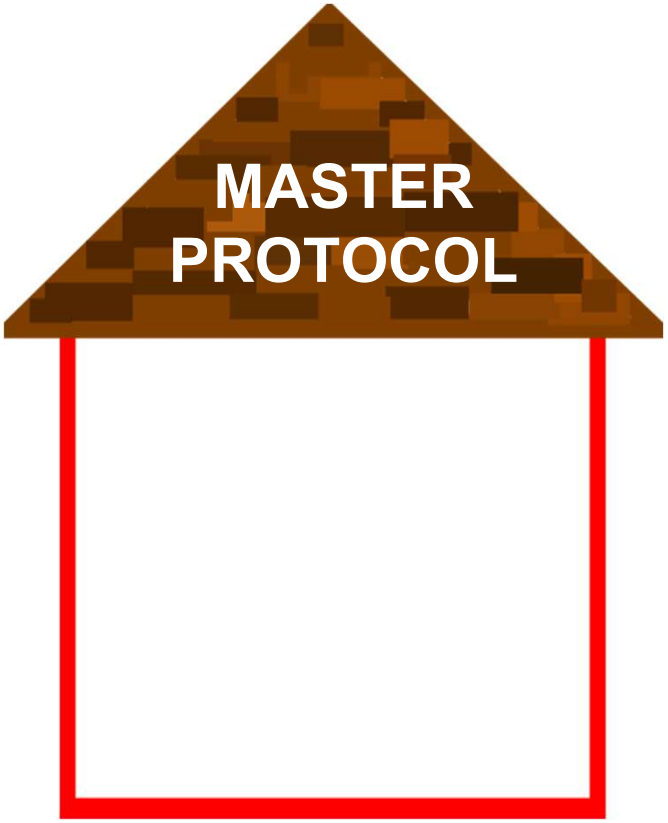
Cuts time in 1/2

Cuts costs by 1/3



Reduces placebo

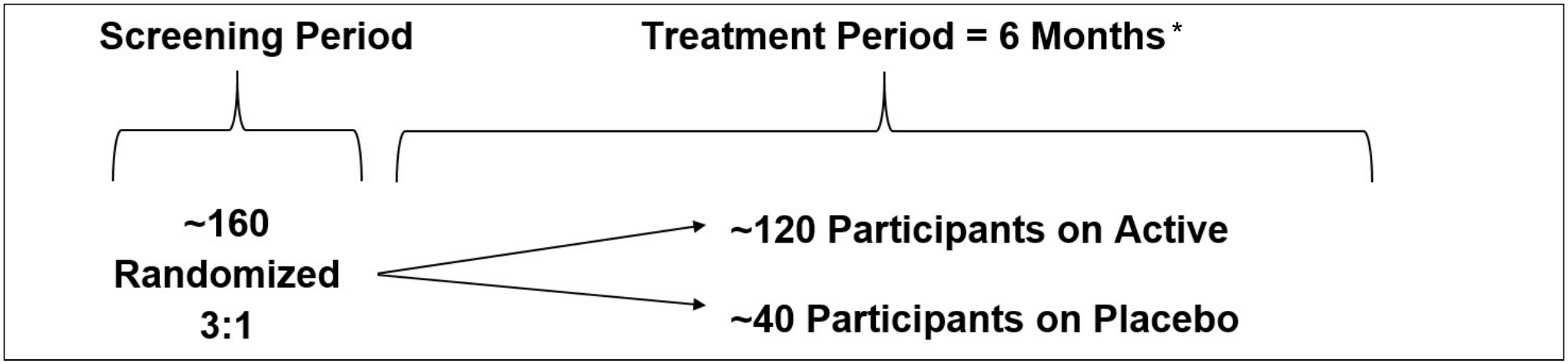
The Platform Trial is Governed by a Master Protocol, a Common Protocol for Multiple Regimens



Key Master Protocol Elements:

- **Target Population**
- **Endpoints**
- **Sample Size**
- **Treatment Duration**
- **Randomization Ratio**
- ***Placebo Sharing***
- ***Adaptive Features***
- ***Perpetual Trial***

Master Protocol – Schema for Each Regimen



* Double Blind Period followed by Open Label Extension

Master Protocol – Target Population

Key Inclusion Criteria

- Sporadic or familial ALS (possible, probable, lab-supported probable, or definite by revised EEC)
- Time since onset of weakness due to ALS ≤ 3 years (36 months)
- Slow vital capacity (SVC) ≥ 50% of predicted capacity for age, height, and sex
- Able to swallow
- Participants must either not take riluzole or be on a stable dose of riluzole for ≥ 30 days
- Participants must either not take edaravone or have completed at least one cycle of edaravone

* Selected based on extensive statistical modeling

Master Protocol – Endpoints

Primary Endpoint

Change in disease severity - **ALS Functional Rating Scale-Revised (ALSFRS-R) + Mortality**

Secondary Endpoints

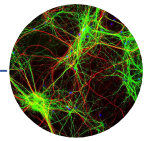
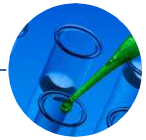
1. Change in respiratory function - slow vital capacity (SVC)
2. Change in muscle strength - hand held dynamometry (HHD)
3. Survival
4. Treatment-specific biomarkers as applicable

Safety Endpoints

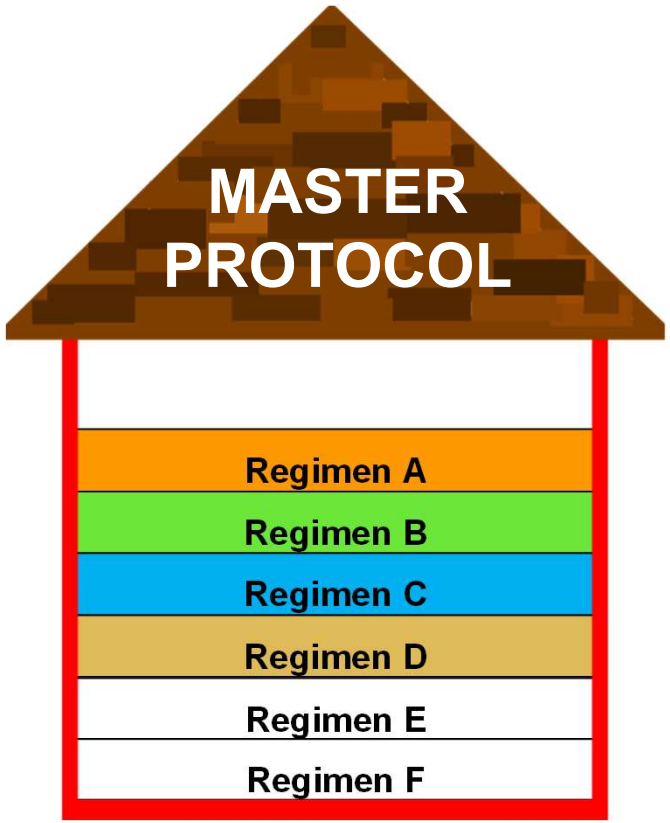
Exploratory Endpoints

Exploratory Endpoints

Endpoint Development Engine

-  **DNA**
-  **Neurofilaments**
-  **Biomarkers** (Blood, Urine, CSF)
-  **Speech Analysis**
-  **Home Spirometry**

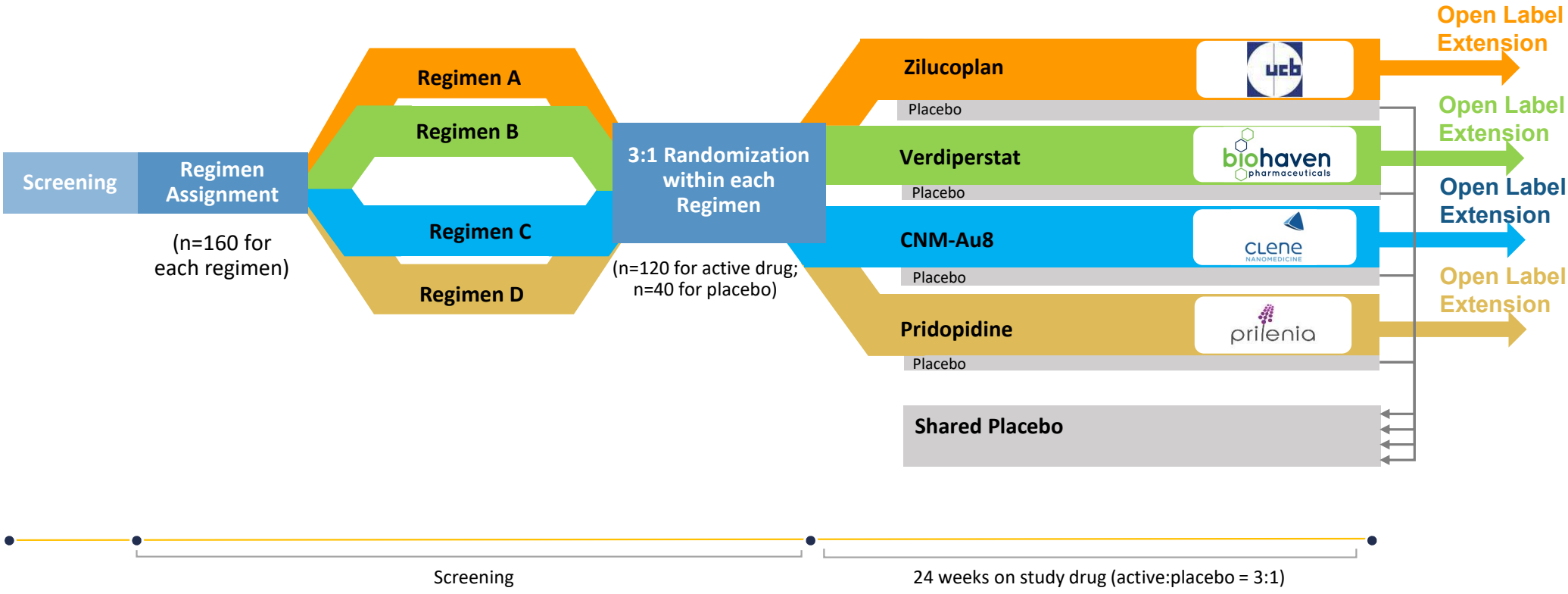
Each Regimen is Described in a Regimen Specific Appendix, an Addendum to the Master Protocol



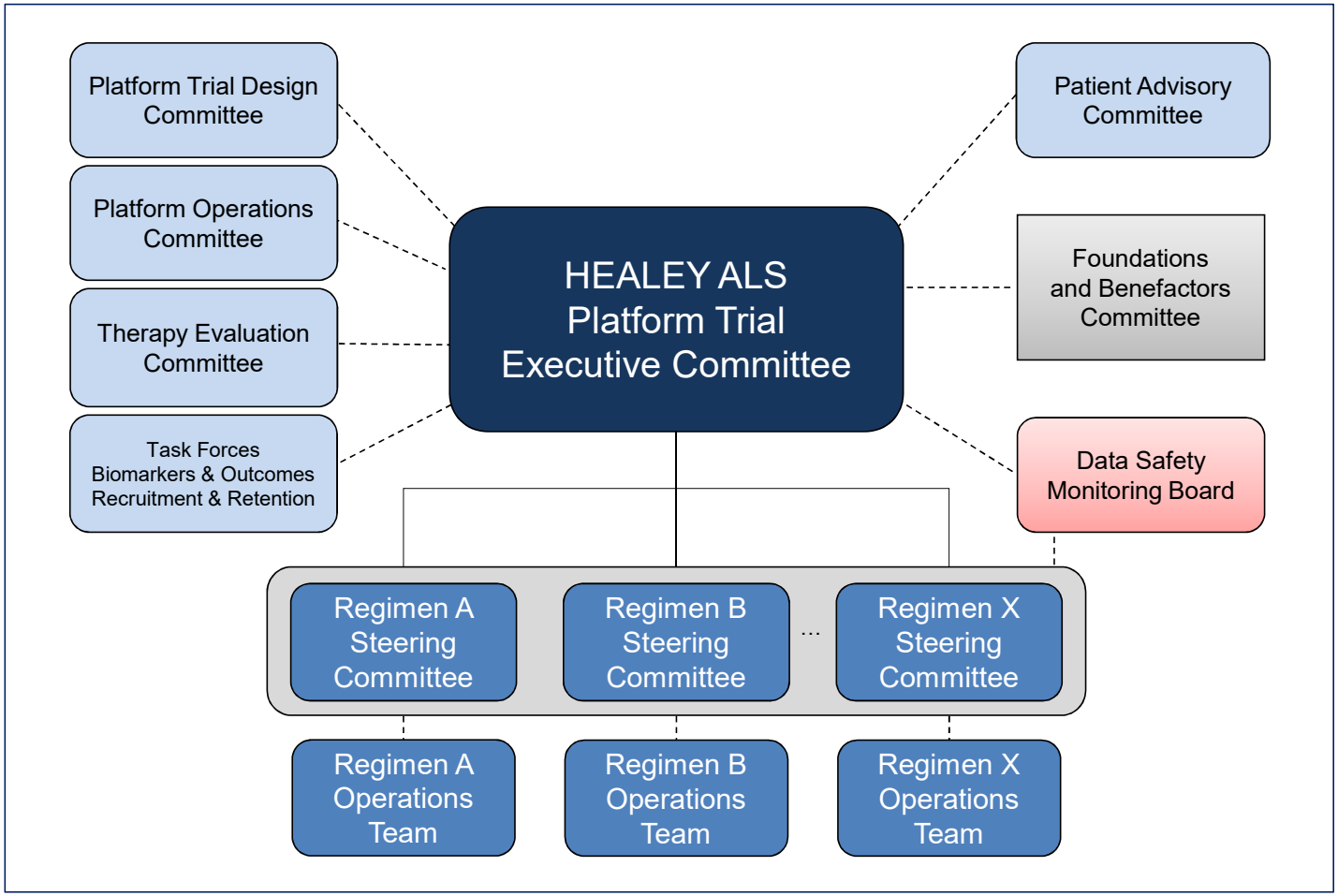
Regimen Specific Appendix Elements:

- Investigational Product Characteristics
- Dosage
- Route of Administration
- Safety Profile
- Additional Assessments, if any
- Additional Inclusion/Exclusion Criteria, if needed for safety

The HEALEY ALS Platform Trial is a Perpetual Adaptive Trial



HEALEY ALS Platform Trial Governance Structure



Platform Trials Change the Pace of Drug Development

The HEALEY ALS Platform Trial:

- The first platform trial for ALS in the world opened in 2020
- Results for the first 4 investigational products are expected about one year after initial launch
- We expect to launch 2-3 new regimens each year

Info: www.massgeneral.org/neurology/als/research/research-partners

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Healey Center
Sean M. Healey & AMG Center for ALS at Mass General

Melanie Quintana

Director and Senior Statistical Scientist

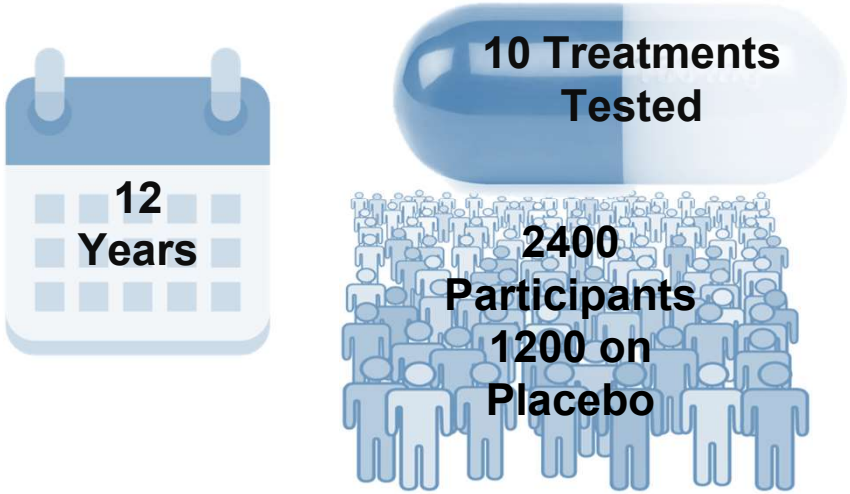
Berry Consultants

Efficiencies in Adaptive/Platform Trials

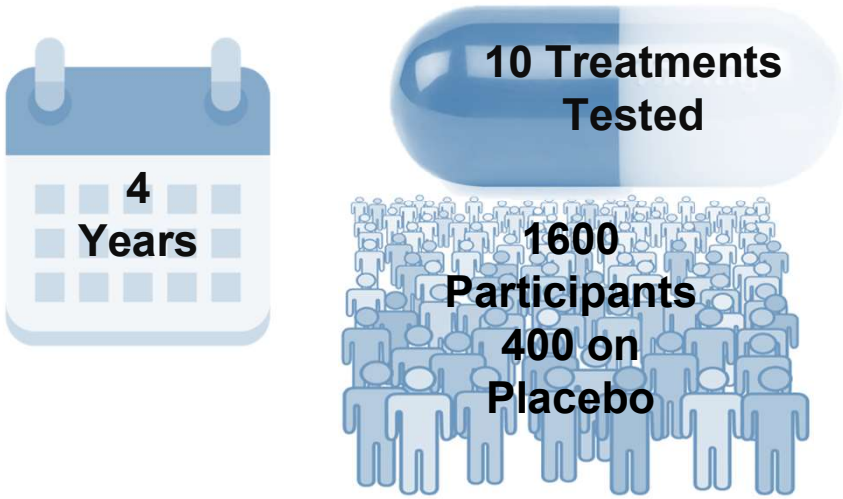
Melanie Quintana, PhD
Director & Senior Statistical Scientist
Berry Consultants

ALS Example: When will we find first effective therapy?

- **Traditional Drug Development**
  - Sequence of fixed 1:1 trials
  - Each N=240 (120 vs. 120)
  - Lag of 3 months between trials



- **Adaptive Platform Trial**
  - Perpetually enrolling max. of 3 regimens
  - Max N=160 (120 vs. 40)
  - Shared controls across regimens



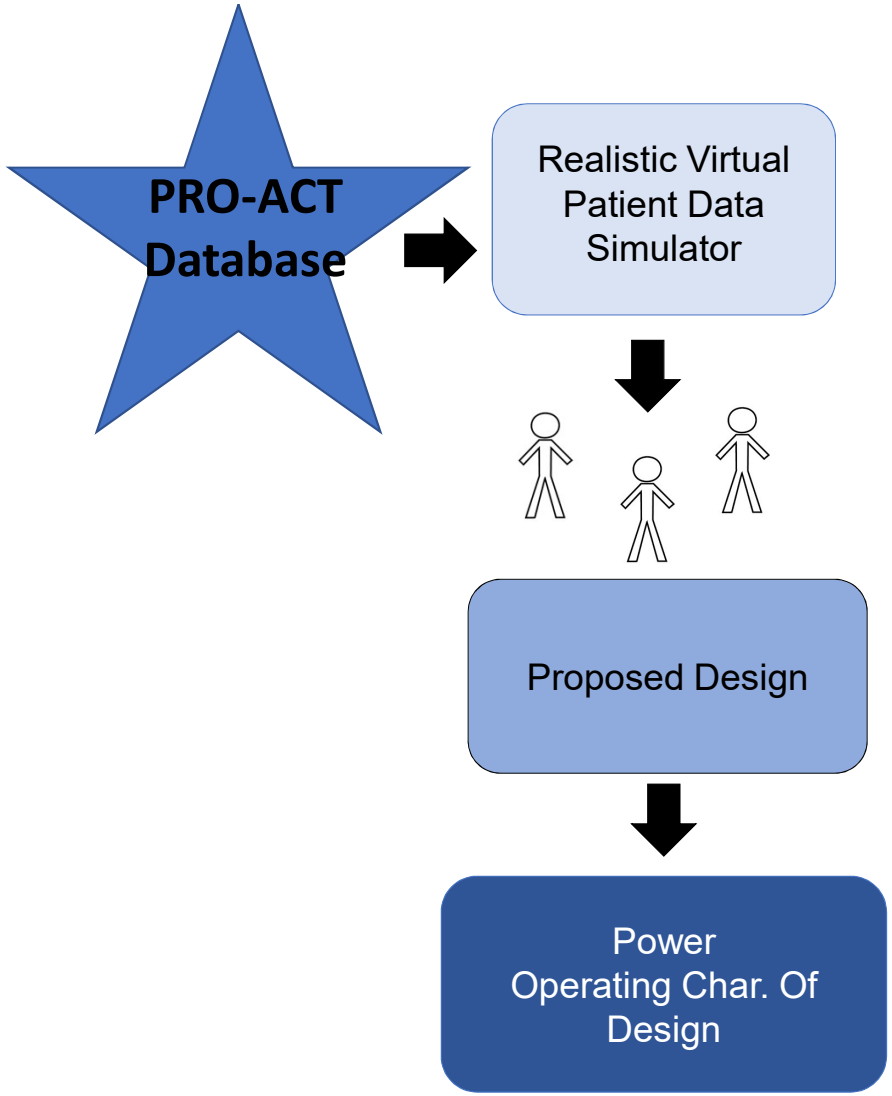
**Assumes 10% of therapies tested are effective with a 30% slowing in rate of progression*

Adaptive/Platform Statistical Efficiencies

- ***Shared controls*** allow higher power with fewer participants on control
- ***Adaptive features*** allow us to screen more agents faster and quickly reject ineffective therapies
  - Shorter trial durations & fewer patients enrolled
- Careful considerations
  - Shared controls require ***similar patient populations*** & ***robust analysis methods*** that can adjust for potential differences across shared control
  - Pre-specification of adaptive rules with good operating characteristics -- ***Simulate, simulate, simulate!***

Clinical Trial Simulation

- Understand operating characteristics of proposed design
- Optimize design under key trial parameters
- Quantify efficiencies



Jeremy Shefner

Kemper and Ethel Marley Professor, Chair of Neurology

Senior Vice President

Barrow Neurological Institute

Richard Bedlack

Director, Duke ALS Clinic

Professor of Neurology

Duke University

Virtual ALS Trials: 10 Lessons Learned and a Path Forward

Richard Bedlack MD PhD

Duke University

Outline

- Definition & examples
- 10 lessons I have learned so far about virtual ALS trials
- Where these can take us in the future

Definition

- A virtual trial is one that evaluates the effects of a drug or device with few or no required in-person visits

- There are several recent examples in ALS
  - PLM Lithium Trial *(Nature Biotechnology 2011;29:411-414)*
  - R.O.A.R.-Lunasin Trial *(Amyotroph Lateral Scler Frontotemporal Degener 2019;20:285-293)*
  - NIH HERV-K Suppression Trial *(NCT02437110)*
  - R.O.A.R-Theracurmin trial *(NCT04499963)*

Lesson 1: There is a need for virtual trials (now more than ever!)

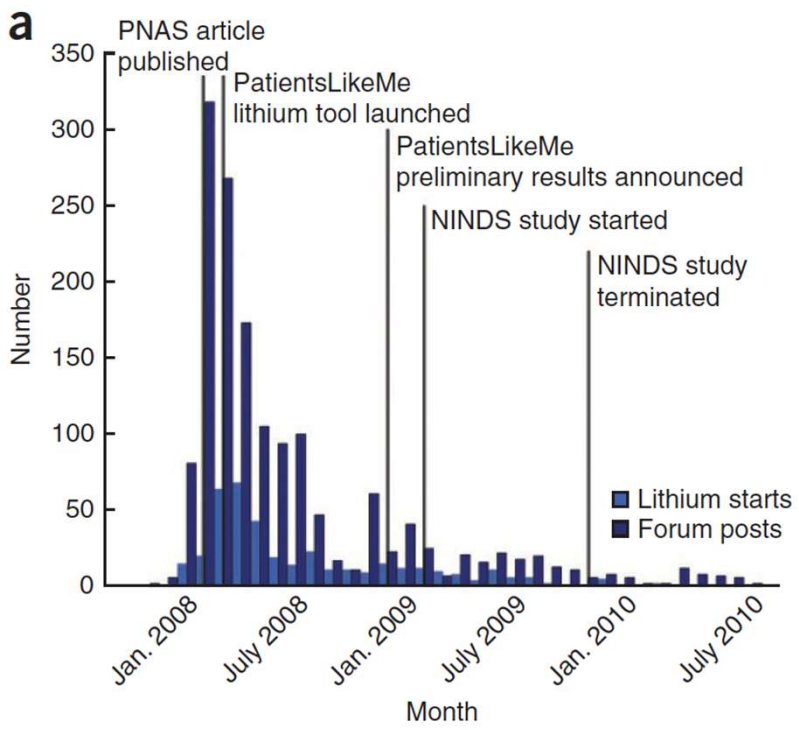
- Travel burdens for PALS can be enormous
  - *Amyotrophic Lateral Scler Frontotemp Degen 2018;19:126-133*
  - *Amyotroph Lateral Scler 2010;11:502-507*
- Travel burdens are one of the main reasons that patients decline to enroll in or drop out of trials
  - *Amyotroph Lateral Scler 2010;11:502-507*
- During a pandemic, in person visits can become unsafe or even impossible
  - Many traditional trials halted

Lesson 2: They can have better enrollment & retention rates than more traditional trials

Trial Type	Enrollment Rate (patients/site/month)	Retention Rate (% of surviving patients who complete all visits)
Traditional	2.2 *(Amyotroph Lateral Scler 2008;9:257-265)*	78% *(Neurology. 2013;81:1350–5)*
Virtual	9.1 *(Amyotroph Lateral Scler Frontotemporal Degen 2019;20:285-293)*	84% *(Amyotroph Lateral Scler Frontotemporal Degen 2019;20:285-293)*

Lesson 3: They can start and be completed faster and with less expense than more traditional trials

- PLM virtual trial of lithium started within 3 months of PNAS article, was completed 9 months later (NINDS lithium trial took more than a year to start, another year to get results)
  - *Nature Biotechnology 2011;29:411-414*
- Lunasin trial (50 patients, 1-year f/u, clinical and biomarker outcomes) cost $250K (comparable traditional trials would cost 5-10x this much)
  - *Amyotroph Lateral Scler Frontotemporal Degener 2019;20:285-293*



Lesson 4: They can enroll a more “real world” population

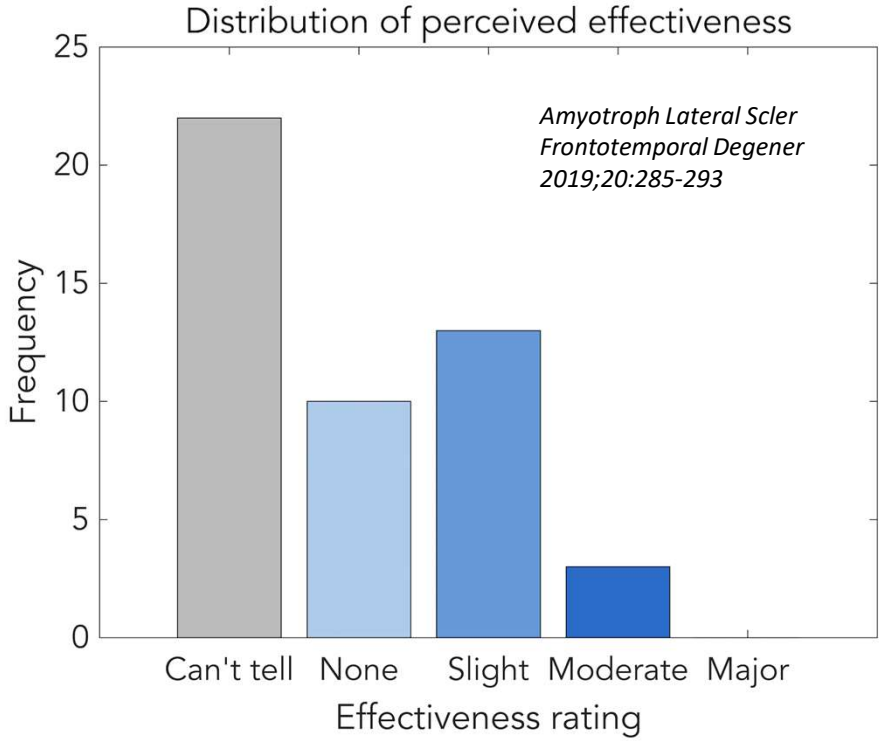
- Traditional trials tend to enroll younger, healthier, faster progressing patients
  - Not representative of patients in ALS clinics *(Neurology 2011;77:1432–7)*

- Virtual trials can have wider range of ages, disease severity, progression *(Amyotroph Lateral Scler Frontotemporal Degener 2019;20:285-293)*
  - Ex. Lunasin trial had some patients with disease duration >10 years, several with NIV, trach, PEG
  - More similar to patients in clinics
  - Results more likely to generalize

Lesson 5: There are good existing options for efficacy measures

- Patient ”Perceived Effectiveness”
  - Part of PLM (used in Lunasin and Theracurmin trials)

- ALSFRS-R
  - Primary in all 4 virtual trials
  - With training, can be accurately measured and recorded by patients *(Amyotroph Lateral Scler Frontotemporal Degener 2019;20:285-293)*
  - More frequent measurements can reduce noise, improve sensitivity (Ann Clin Transl Neurol. 2020 Jul; 7(7): 1148–1157)



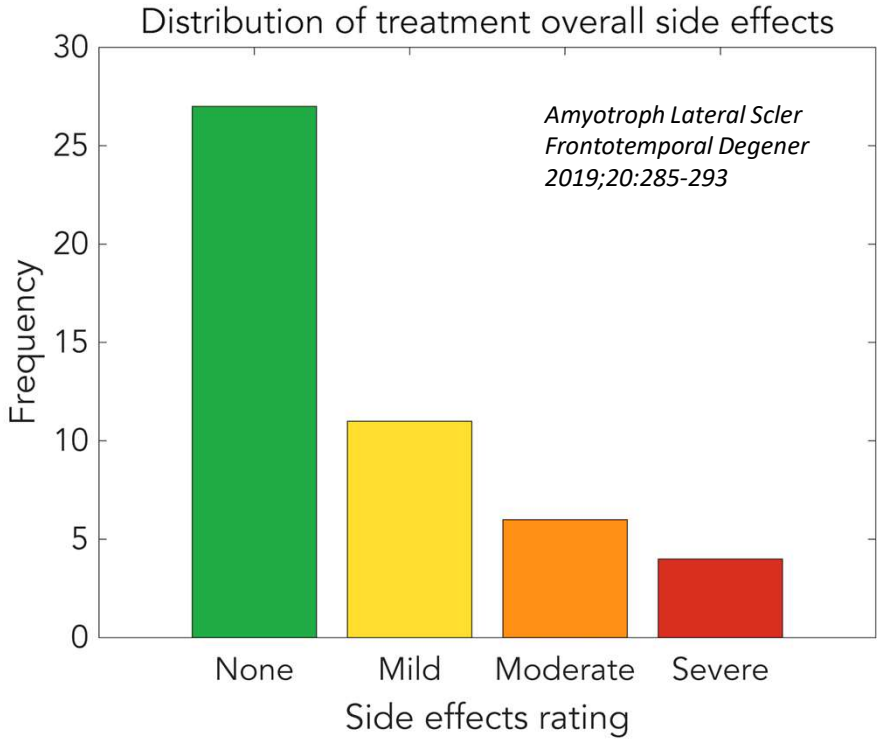
Lesson 6: There are exciting emerging options for efficacy measures

- PLM “Thrive” questionnaire
  - Used in Theracurmin trial
- Home VC, home hand grip dynamometry, remote EIM, wearables, remote speech analytics
  - As with ALSFRS-R, more frequent measurements result in less noise, improved sensitivity *(Ann Clin Transl Neurol. 2020 Jul; 7(7): 1148–1157)*

Lesson 7: There are existing options for safety measures

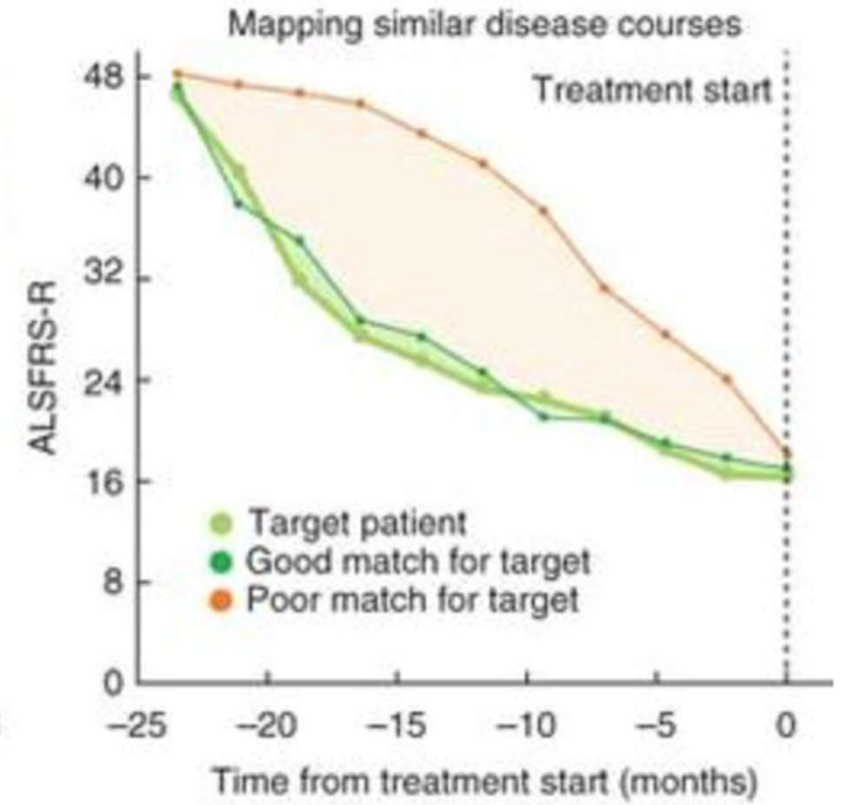
- Patient “Perceived Side Effects”
  - Part of PLM, used in Lunasin and Theracurmin trials
- Coordinator telephone screening for adverse events
  - Used in Lunasin and Theracurmin trials
- Home blood draws
  - Used in HERV-K Suppression Trial

- But: I still feel more confident in safety monitoring when I can see and examine patients



Lesson 8: There are good options for controls

- Historical (ex. PLM method)
  - For each treated patient, 3 controls matched according to pre-treatment ALSFRS-R progression *(Nature Biotechnology 2011;29:411-414)*
  - Used in PLM Lithium trial, Lunasin and Theracurmin trials
- Predictive modelling
  (*Neurotherapeutics* 2015;12:417–423)
- Concomitant (used in part of Duke Theracurmin trial)



Lesson 9: PLM can be very helpful

- Existing infrastructure allows patients to enter ALFRS-R, perceived effectiveness, perceived side effects, perceived burdens, perceived adherence
- With more than 12,000 registered PALS contributing longitudinal data, great ability to generate matched historical controls
- Data publicly available throughout a trial
- Motivated and reliable partner in my Lunasin, Theracurmin trials

Lesson 10: Clinician oversight still needed

- Informed consent
- Diagnosis confirmation
- Outcome training
- Adverse event screening, classification, reporting
- Adherence/compliance monitoring, prompting

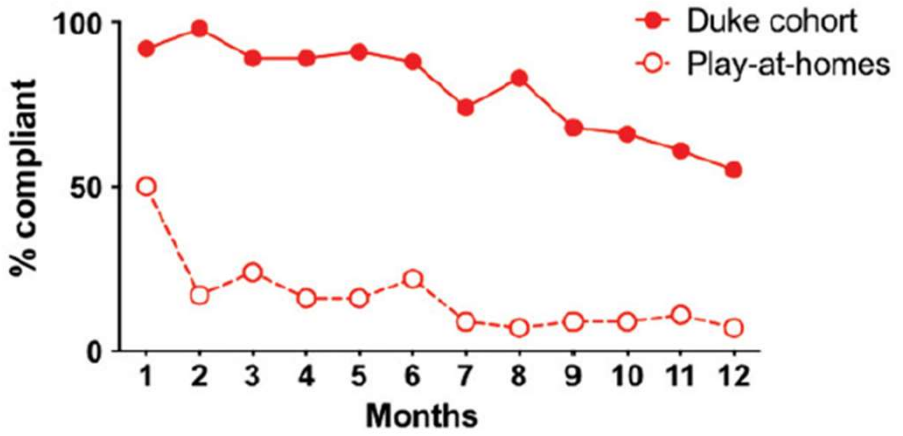


Figure 7. Adherence in participants versus those "playing along at home". This figure shows that participant adherence (% completing at least 2 out of 3 PLM outcome measures) was high for the first 6 months of the study, then dropped off after that (solid line). On the other hand, a "play along at home" cohort (54 PLM users who started self-experimentation with Lunasin during our trial enrollment period) had much lower adherence (dashed line).

Future Directions

- Virtual trials cannot yet completely replace more traditional ones
  - Safety monitoring not as thorough
- Stand alone virtual trials best for studying GRAS products (ex. supplements)
- Virtual adjuncts to more traditional trials
  - Phase 4 trials
  - Expanded access programs of safe products

Philip Green

ALS Research Ambassador

Duke | MARGOLIS CENTER *for* Health Policy

Lei Xu

Chief of General Medicine Branch 2

Division of Clinical Evaluation and Pharmacology/Toxicology

U.S. Food and Drug Administration

Teresa Buracchio

Deputy Director

Division of Neurology 1

U.S. Food and Drug Administration

Session 2 | Discussion Questions

1. What steps can be taken make therapeutic development for ALS more efficient while ensuring the collection of robust clinical data to support regulatory and clinical decision making?

2. What benefits can remote monitoring and decentralized trials bring to researchers and patients? What are the barriers to increasing the use of remote monitoring and decentralized trials?

3. What steps can be taken to increase patient enrollment in innovative clinical trials? What are successful examples of this? What are the barriers?

4. How can trials be designed to best support patient access and subgroup analysis?

Day 1 Adjournment & Day 2 Instructions

Mark McClellan, MD, PhD

Director, Duke-Margolis Center for Health Policy

Improving Basic Research, Clinical Trial Infrastructure, and Community Engagement to Support Drug Development for ALS

Day 2 – Thursday, January 28th

Virtual Private Workshop — January 27 & January 28, 2021

Welcome & Overview of Day 2

Mark McClellan, MD, PhD

Director, Duke-Margolis Center for Health Policy

Session 3: Research Infrastructure and Data Sharing for ALS

12:05pm – 1:05pm

Alexander Sherman

Director

Center for Innovation and Bioinformatics

MGH Neurological Clinical Research Institute

Duke-FDA Workshop on Basic Research, Clinical Trial Infrastructure, and Community Engagement to Support Drug Development for ALS

Duke | MARGOLIS CENTER for Health Policy

FDA U.S. FOOD & DRUG ADMINISTRATION

Research Infrastructure and Data Sharing in ALS

Center for Innovation and Bioinformatics

Neurological Clinical Research Institute

avsherman@mgh.harvard.edu

www.data4cures.org

January 28, 2021

NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

Research Infrastructure for Big Data

Big Data Inventory
International inventory of Big Data resources in ALS https://www.data4cures.org/resources

Work Groups/Committees
Big Data Committees (**Sustainability, Genomics, Biobanking, Imaging**, and **Data Access)**

Collaborations in Patient Identification for Future Information Exchange
Utilizations of Unique Identifiers in basic research, clinical studies and trials

NeuroBANK® ALS Ecosystem
6051 pALS from **23** clinical studies, **80+** clinical sites, **14** countries, **108K+** vials of biofluids, **3.4K** DNA samples

ALS/MND Natural History Consortium
Enrollment from 9 member-sites 1541 people with ALS/MND

ALS/MND Patient Portals (Patient-Reported Outcome Measures)
ALS Focus
Everything ALS

PRO-ACT/PRO-ACE
Pooled **R**esource **O**pen-**A**ccess **C**linical **T**rials/clinical r**E**search databases

NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

BIG Data in ALS/MND Committee

The **BIG Data in ALS/MND** committee's interests comprise broad spectrum of projects in supporting international patient-centric approaches in clinical research, from developing recommendations and specifications for existing and new regulatory-compliant platforms, to unique research participants' identification, to identifying new sources of clinical and research data, to data capture, analyses, visualization, and distribution, to sharing best practices, research protocols, and research agreements

Big Data Committees with national and international representation, focus on identifying global ALS resources, creating and promoting common practices and regulatory-compliant language, creating internationally-applicable SOPs for collection and sharing of information, and a single set of policies for data sharing addressing regulatory, IP, dissemination, and publication concerns:

- **Sustainability**
- **Genomics**
- **Biobanking**
- **Imaging**
- **Data Access**

Big Data Inventory

https://www.data4cures.org/resources

RESOURCE	WEB SITE	TYPE
NeuroGUID server	http://www.NeuroGUID.org	Patient ID
NeuroBANK platform	https://nctu.partners.org/NeuroBANK	Real World Data (RWD)
ALS Living Library NEALS Biobank	www.neals.org/for-als-researchers/neals-sample-repository/	Biobank - Biofluids
New York Genome Center	www.nygenome.org/als/	DNA
Institute of Genetic Medicine	www.igm.columbia.edu/	DNA
Cedars-Sinai iPSC Core	www.cedars-sinai.edu/Research/Departments-and-Institutes/Regenerative-Medicine-Institute/	iPSC
NeuroLINCS iPSC / omics collaborative	http://neurolincs.org/	omics
Target ALS human PM tissue inventory	http://www.targetals.org/inventory_search.html	Biobank - PM
Project MinE full DNA profiles	https://www.projectmine.com/	DNA, RWD
PRO-ACT clinical trials' dataset	http://www.alsdatabase.org	RCT Data
PRO-ACE observational studies' dataset	https://www.data4cures.org/pro-ace	Real World Data (RWD)
NiSALS – Neuroimaging Society in ALS	https://nisals.net/	Images, RWD
Harvard NeuroVERSE	https://dataverse.harvard.edu/dataverse/NeuroVERSE	DOIs for ALS datasets
ALS Focus	http://www.alsfocus.org	Patient-Reported Outcomes
EverythingALS	https://www.everythingals.org/	Patient-Reported Outcomes
1-855-ASK-NEURO Helpdesk	https://www.data4cures.org/collaborate	Support

Big Data Sustainability Committee

Organization	Leader
The ALS Association	Neil Thakur
The Canadian ALS Association	David Taylor
Motor Neurone Disease Association (UK)	Brian Dickie
The Les Turner ALS Foundation	Andrea Pauls Backman
The ALS Hope Foundation	Terry Heiman-Patterson





NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

Genomics Committee

Organization	Leader
New York Genome Center	Dr. Hemali Phatnani
IGM/Columbia	Dr. Mathew Harms
Project MinE	Dr. Jan Veldink
University of Massachusetts	Dr. John Landers
Kings College	Dr. Amar Al-Chalabi





NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

Big Data Inventory

https://www.data4cures.org/resources

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New York Genome Center	www.nygenome.org/als/	DNA
Institute of Genetic Medicine	www.igm.columbia.edu/	DNA
Cedars-Sinai iPSC Core	www.cedars-sinai.edu/Research/Departments-and-Institutes/Regenerative-Medicine-Institute/	iPSC
NeuroLINCS iPSC / omics collaborative	http://neurolincs.org/	omics
Target ALS human PM tissue inventory	http://www.targetals.org/inventory_search.html	Biobank - PM
Project MinE full DNA profiles	https://www.projectmine.com/	DNA, RWD
PRO-ACT clinical trials' dataset	http://www.alsdatabase.org	RCT Data
PRO-ACE observational studies' dataset	https://www.data4cures.org/pro-ace	Real World Data (RWD)
NiSALS – Neuroimaging Society in ALS	https://nisals.net/	Images, RWD
Harvard NeuroVERSE	https://dataverse.harvard.edu/dataverse/NeuroVERSE	DOIs for ALS datasets
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Big Data Inventory

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New York Genome Center	www.nygenome.org/als/	DNA
Institute of Genetic Medicine	www.igm.columbia.edu/	DNA
Cedars-Sinai iPSC Core	www.cedars-sinai.edu/Research/Departments-and-Institutes/Regenerative-Medicine-Institute/	iPSC
NeuroLINCS iPSC / omics collaborative	http://neurolincs.org/	omics
Target ALS human PM tissue inventory	http://www.targetals.org/inventory_search.html	Biobank - PM
Project MinE full DNA profiles	https://www.projectmine.com/	DNA, RWD
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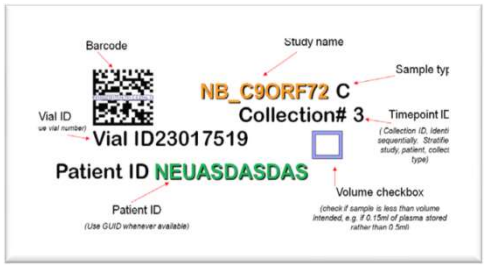
EverythingALS	https://www.everythingals.org/	Patient-Reported Outcomes
1-855-ASK-NEURO Helpdesk	https://www.data4cures.org/collaborate	Support

NEALS ALS Consortium BioRepository

Bob Bowser

James Berry

Biofluid	# Participants	# Vials
DNA	3392	10800
CSF	434	6901
Plasma	1706	63707
Serum	1735	19636
PBMC (iPSC)	2346	7203



https://www.neals.org/for-als-researchers/neals-sample-repository/

NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

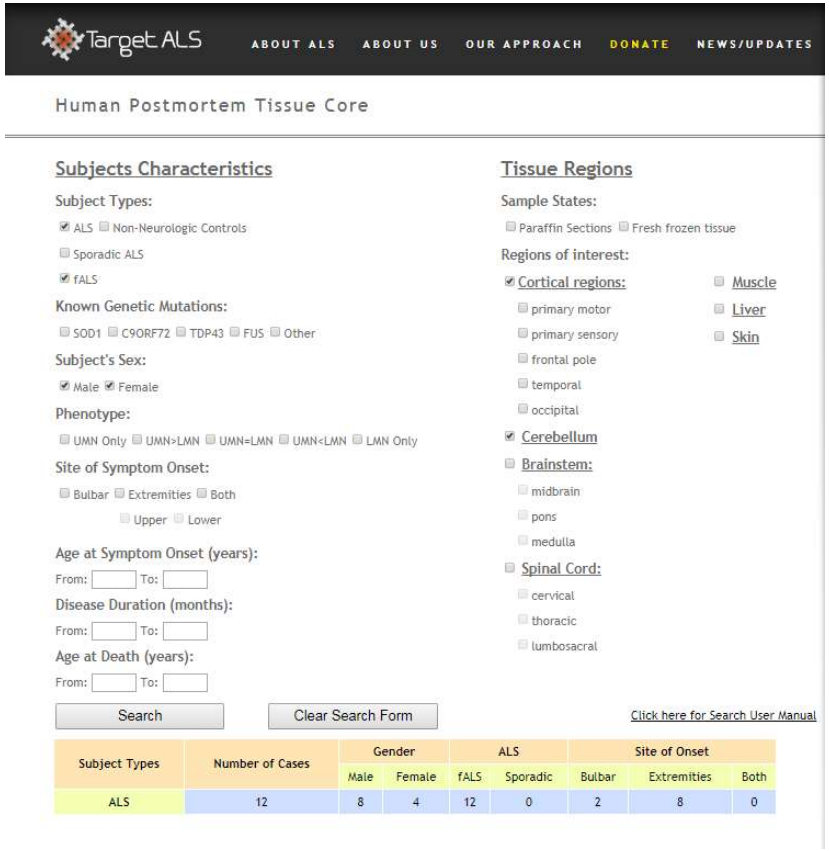
Target ALS Human Postmortem Tissue Core

Biospecimen	# Participants	# Samples
Post-mortem tissues	253 cases	~18K tissues

http://www.targetals.org/inventory_search.html

Lyle Ostrow

Manish Raisinghani



NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

Collaborations in Patient Identification for Information Exchange

http://www.NeuroGUID.org

Neurological Global Unique Identifier

GUIDE your Neuro research with NeuroGUID™!

- The Center for Disease Control's **National ALS Registry** generated 5K+ NeuroGUIDs /NeuroSTAmPs from pALS population with 10%+ having data in NeuroBANK-based studies
- Clinical Trials (**Platform Trial**, **CENTAUR, VITALITY**) utilize NeuroGUIDs/NeuroSTAmPs
- **ALS Focus** and **EverythingALS** patient platforms utilize NeuroSTAmPs for pALS, caregivers, and controls
- **New York Genome Center** and **Institute of Genetic Medicine** use NeuroGUIDs/ NeuroSTAmPs for DNA files identification
- **NeuroGUID** Platform was a **2020 Bio-IT World Innovative Practices Awards Winner** as "outstanding example of how technology innovations and strategic initiatives can be powerful forces for change in the life sciences, from basic biomedical research to drug development and beyond"

NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

NeuroBANK® ALS Ecosystem

alsFINDINGaCURE™

ALS ASSOCIATION
Create a world without ALS.

NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

- EHR
- Observational Studies
- Bio Banks
- Image Banks
- PRO
- Genetics
- Omics
- Cell Lines
- Mobile Apps

Tools/Platforms

- **NeuroGUID™**
  Neurological Global Unique Patient ID
- **NeuroBANK®**
  Accelerated Research Environment
- **NeuroBIO™**
  Distributed BioRepository
- **NeuroPRO™**
  Patient-Reported Outcomes (Portal)
- **NeuroCHARTS™**
  Analytical Tools

Patients == Research Participant

NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

NEUROBANK®

NeuroBANK® ALS Ecosystem

#	Projects	CLN	CGN	NTR	BFL	PMT	IMG	DNA	RNA	iPSC	EHR	PRO	MOB
1	C9orf72	Y			Y			Y		Y			
2	Iron Horse	Y			Y								
3	TRACK ALS	Y			Y		Y	Y	Y	Y			
4	VITALITY	Y			Y								
5	Answer ALS	Y			Y		Y	Y	Y	Y			Y
6	GTAC	Y	Y		Y			Y	Y	Y			
7	Postmortem Tissue Bank	Y			Y	Y		Y	Y				
8	Natural History in ALS/MND	Y	Y		Y			Y	Y		Y	Y	
9	EAT MORE	Y		Y									
11	CABB	Y			Y			Y	Y				
12	Microbiome in ALS	Y		Y	Y							Y	
13	UMN Registry	Y			Y								
14	Lunasin ALS Reversals	Y										Y	
15	Digital Quantitative Measurements (Digital ALS)	Y											Y
16	Cognitive-behavioral Symptoms (ALS/FTD)	Y	Y				Y						
17	Fluid Biomarkers/Deep Phenotyping	Y	Y		Y			Y	Y				
18	Providence ALS Patient Registry	Y	Y								Y		
19	C9orf72 Genomic Assessment Protocol (C9GAP)	Y			Y			Y				Y	
20	Target ALS Fluid Biomarkers	Y			Y	Y		Y					
21	Symptom Monitoring in Real Time (SMART)	Y	Y										Y
22	The Dominant Inherited ALS (DIALS) Network	Y	Y		Y			Y	Y	Y			
	TOTAL STUDIES	**22**	**7**	**2**	**15**	**2**	**3**	**11**	**8**	**5**	**2**	**4**	**3**

CLN	Clinical and phenotypical data	**CGN**	Cognitive assessment	**NTR**	Dietary/Nutrition
BFL	Biofluids (CSF, Plasma, Serum)	**PMT**	Post-mortem tissues	**IMG**	Imaging
DNA	DNA (WGS)	**RNA**	RNA	**iPSC**	Cell lines
EHR	EHR Integration	**PRO**	Patient-reported outcomes (PRO)	**MOB**	Integration with mobile apps

NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

NEUROBANK®

NeuroBANK® ALS Ecosystem

- **23** ALS-related research projects
- **83** participating sites from **14** countries with **436** NeuroBANK-trained personnel
- **6051** people with ALS and controls
- **493 (8.1%)** volunteers participate in more than one study
- **15** volunteers participate in **4+** (!), **6** in **5+** (!!), and **1** in **6**(!!!) research projects
- **3392** DNAs samples collected for WGS
- **2346** PBMC samples collected for cell lines generation
- **253** cases of postmortem tissue collection (18K tissue samples)
- **108K+** vials of biofluids are in NeuroBIO™ virtual biobank

Biofluid	# Participants	# Vials
DNA	3392	10800
CSF	434	6901
Plasma	1706	63707
Serum	1735	19636
PBMC (iPSC)	2346	7203
Post-mortem tissues	253 cases	~18K tissues

NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

NEUROBANK®

REAL WORLD DATA

Patients == Research Participant

- EHR
- Observational Studies
- Bio Banks
- Image Banks
- PRO
- Genetics
- Omics
- Cell Lines
- Mobile Apps

Tools/Platforms

NeuroGUID™
Neurological Global Unique Patient ID

NeuroBANK™
Accelerated Research Environment

NeuroBIO™
Distributed BioRepository

NeuroPRO™
Patient-Reported Outcomes (Portal)

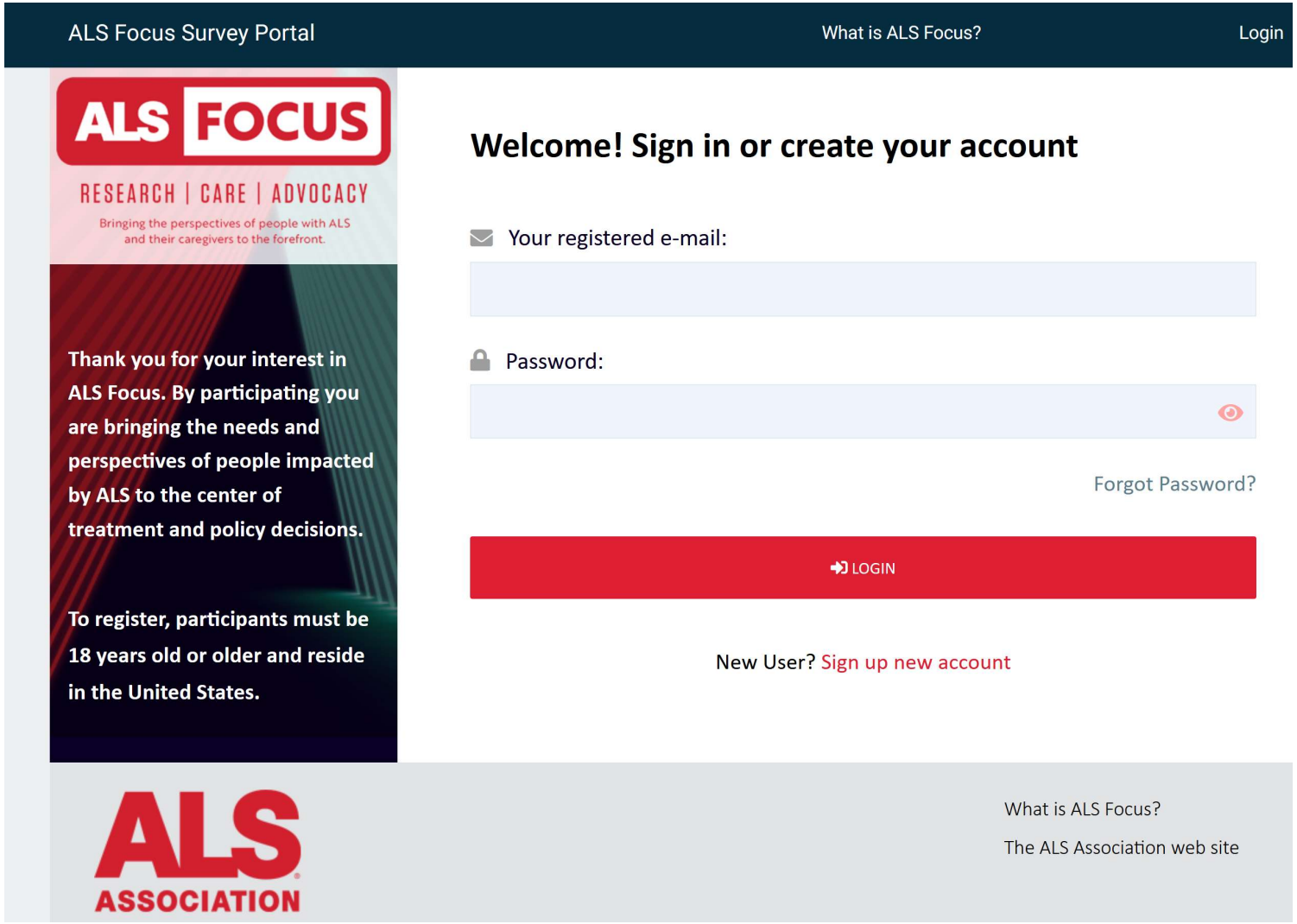
NeuroCHARTS™
Analytical Tools

NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

Sarah Parvanta

Sellam Birhane

Neil Thakur



NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

ALS FOCUS

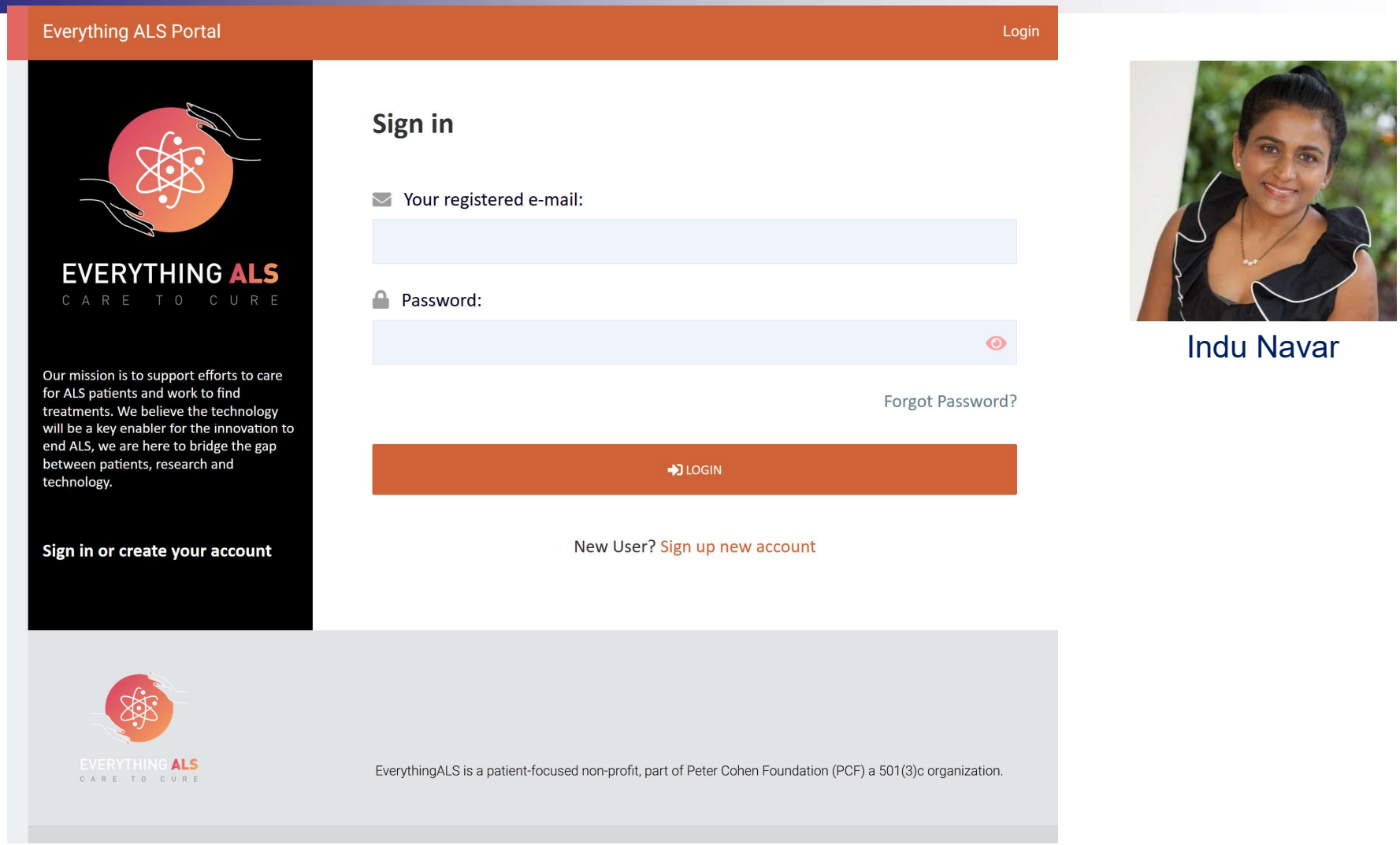
BRINGING THE PERSPECTIVES OF PEOPLE WITH ALS AND THEIR CAREGIVERS TO THE FOREFRONT OF RESEARCH, CARE, AND ADVOCACY.

ALS Focus surveys to date

- **~1500 Members** (pALS and Caregivers)
- **Survey on Insurance Needs and Financial Burdens**
  - N=**419** people with ALS and caregivers
- 'About Me' **Demographics/Dx History** Survey
  - Ongoing
  - N≈**~1,000** people with ALS and caregivers
- Survey on **What Matters Most**
  - Based on ALS Health Index developed by Chad Heatwole at the University of Rochester
  - N≈**685** people with ALS and caregivers
- **Health Status Survey**
  - Ongoing
  - N≈**257** people with ALS

NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

ALS ASSOCIATION



Indu Navar

NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

Big Data and Machine Learning in ALS

ALS ASSOCIATION

PRO-ACT

Welcome to the
Pooled Resource Open-Access ALS Clinical Trials Database

Home | Data | How to Use PRO-ACT | ALS Prize | ALS Links | About Us | Contact Us

PRO-ACT provides users with easy access to:

- Over 10,700 fully de-identified clinical patient records
- Placebo and treatment-arm data from 23 Phase II/III clinical trials
- Demographic, lab, medical and family history, and other data elements
- More than 10 million longitudinally collected data points

Data Sets

Please register to be able to download data.

In building PRO-ACT, as part of our data cleaning process for the lab data, units were converted

Form Name	Subjects	Records	Values	Date/Time
Adverse Events	8628	74545	748566	12/29/2015 7:00:17 PM
ALL FORMS	10723	2869973	12638797	1/4/2016 6:16:08 PM
ALSFRS(R)	6844	60775	791473	12/29/2015 7:00:59 PM
Concomitant Medications	7656	111848	376098	12/29/2015 7:02:27 PM
Death report	4633	4634	8033	12/29/2015 7:02:59 PM
Demographics	10723	10723	39107	12/30/2015 5:02:30 PM
El Escorial criteria	2551	2551	5102	9/2/2020 12:43:02 PM
Family History	1007	1071	2452	12/30/2015 5:03:50 PM
Forced Vital Capacity	8848	48856	200200	1/4/2016 6:14:52 PM
Laboratory Data	8342	2445059	9659191	12/29/2015 7:07:18 PM
Riluzole use	8817	8817	17633	12/29/2015 7:05:18 PM
Slow Vital Capacity	2717	9525	25532	12/29/2015 7:05:51 PM
Subject ALS History	9394	12058	35967	1/4/2016 6:14:09 PM
Treatment Group	9640	9640	16830	12/29/2015 7:06:18 PM
Vital Signs	9973	72422	717715	1/4/2016 6:15:32 PM


Melanie Leitner


Neta Zach


Neil Thakur


Kuldip Dave

- Negotiating with Data Donors
- El Escorial Criteria added
- Incorporated Neuraltus NP-001 Phase II trial's dataset
- PRO-ACT 3-year grant funded by ALS Association

BRING YOUR TRIALS' DATA TO PRO-ACT!!!

NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

Nature Biotechnology **33**, 51–57 (2015) doi:10.1038/nbt.3051

PRIZE4LIFE

PRO-ACT

Impacts of PRO-ACT on ALS R&D

Scientific Benefits:

- ❑ Understanding of natural history and disease heterogeneity
- ❑ Novel biomarkers and pathways of disease
- ❑ 50+ papers and 100+ symposia abstracts

Clinical Development Benefits

- ❑ Simulations
- ❑ Test stratification theories
- ❑ Reduce costs of future ALS clinical trials
- ❑ Explore link between disease progression and medication use

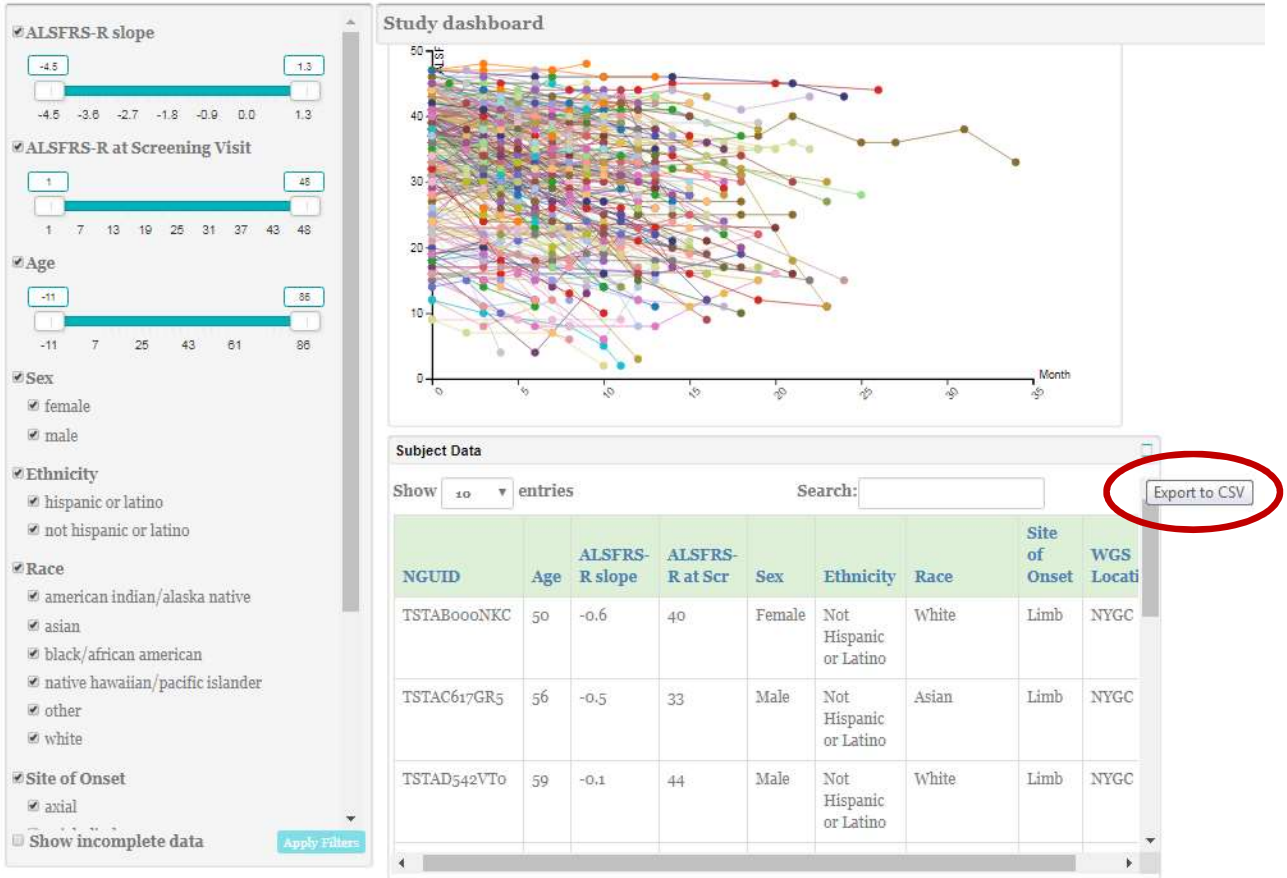
Other Benefits

- ❑ Grow quantitative workforce with interest in/exposure to ALS data

Big Data and Machine Learning in ALS

PRO-ACE: Bring Your Own Data (BYOD)

4K+ patient-records from **observational** studies and clinical visits



NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

ALS/MND Natural History Consortium

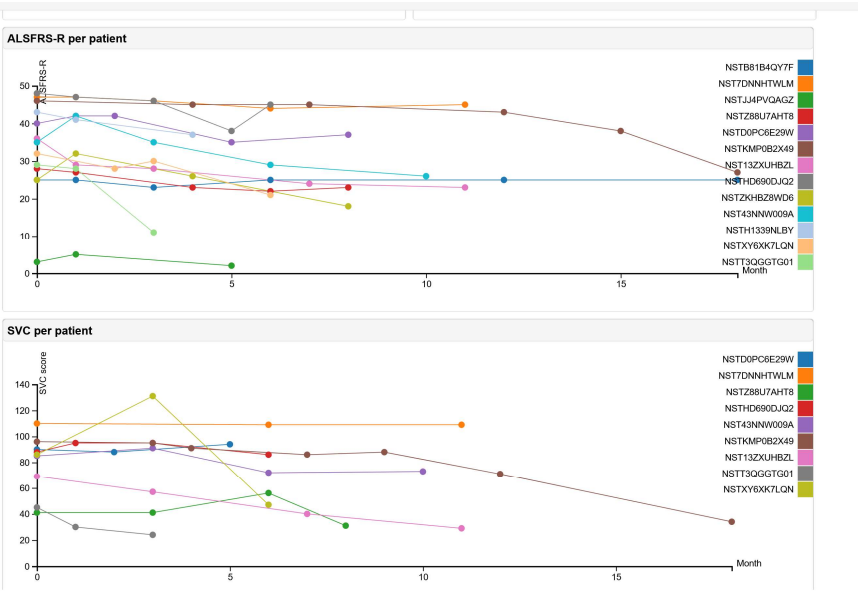
Enrollment from 9 member-sites reached **1561** pALS/MND

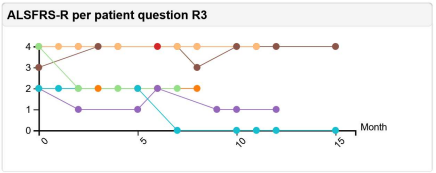
NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

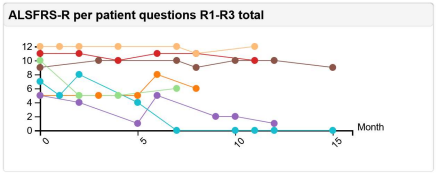
NEUROBANK®

Expanded Access Program in ALS

NeuroREACH™ EAP Platform







ALSFRS-R data table

Show 10 entries Search:

SUBJECT_UID	Site UID	Local UID	Visit	ALSFRS-R Date	ALSFRS-R Total
NSToHCCHTZ9W	701	112	1	10/18/2019	47
NSToHCCHTZ9W	701	112	2	12/17/2019	43
NSToHCCHTZ9W	701	112	3	02/26/2020	41
NSToHCCHTZ9W	701	112	4	04/10/2020	43
NSToHCCHTZ9W	701	112	5	06/12/2020	43
NSToHCCHTZ9W	701	112	6	09/10/2020	41
NST263AoE7RP	701	104	1	04/24/2019	17

SVC data table

Show 10 entries Search:

SUBJECT_UID	Site UID	Local UID	Visit	SVC Date	SVC
NSToHCCHTZ9W	701	112	1	10/18/2019	66
NSToHCCHTZ9W	701	112	2	12/17/2019	52
NSToHCCHTZ9W	701	112	3	02/26/2020	67
NSToHCCHTZ9W	701	112	4	09/10/2020	60
NST263AoE7RP	701	104	1	04/24/2019	46
NST263AoE7RP	701	104	2	12/11/2019	37
NST263AoE7RP	701	104	3	03/11/2020	35

NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

Jane Larkindale

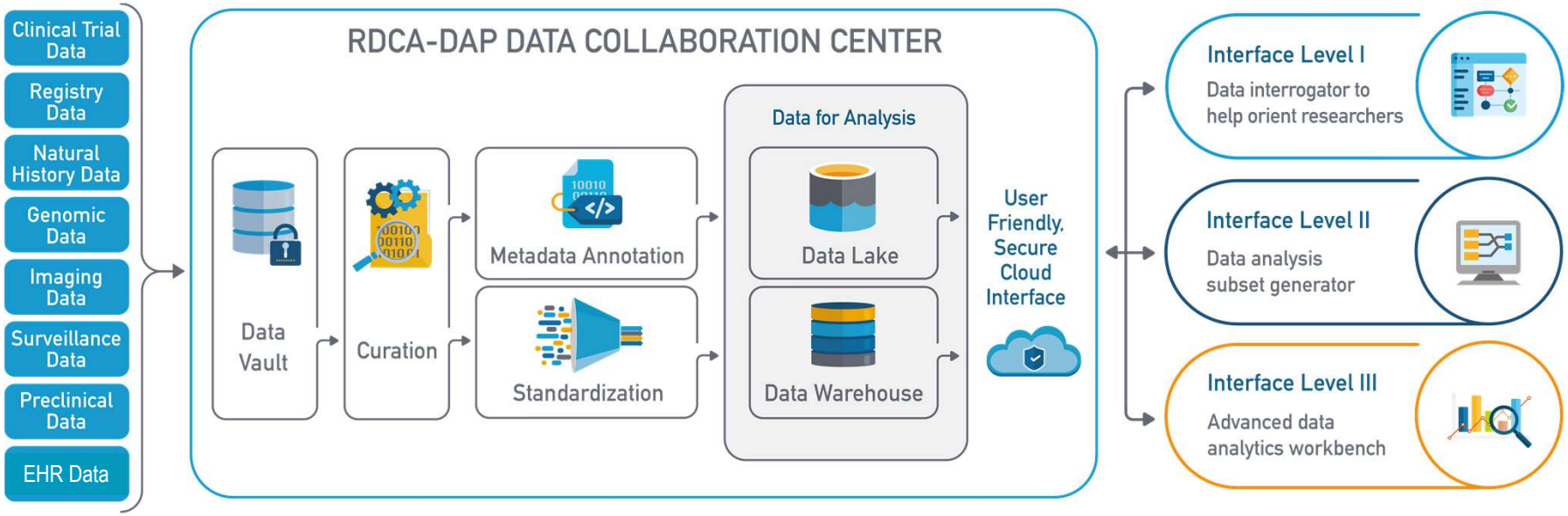
Executive Director

Duchenne Regulatory Sciences Consortium; Rare Disease Cures Accelerator-Data and Analytics Platform

Critical Path Institute

The Rare Disease Cures Accelerator – Data and Analytics Platform

The Rare Disease Cures Accelerator- Data and Analytics Platform (RDCA-DAP) is a neutral, independent data collaboration and analytics hub to promote the sharing of critically important data across rare diseases in order to accelerate the understanding of disease natural history and optimize clinical trial design



Critical Path Institute is supported by the Food and Drug Administration (FDA) of the U.S. Department of Health and Human Services (HHS) and is 69% funded by FDA/HHS, totaling $19,471,171, and 31% percent funded by non-government source(s), totaling $8,612,313. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement by, FDA/HHS or the U.S. Government

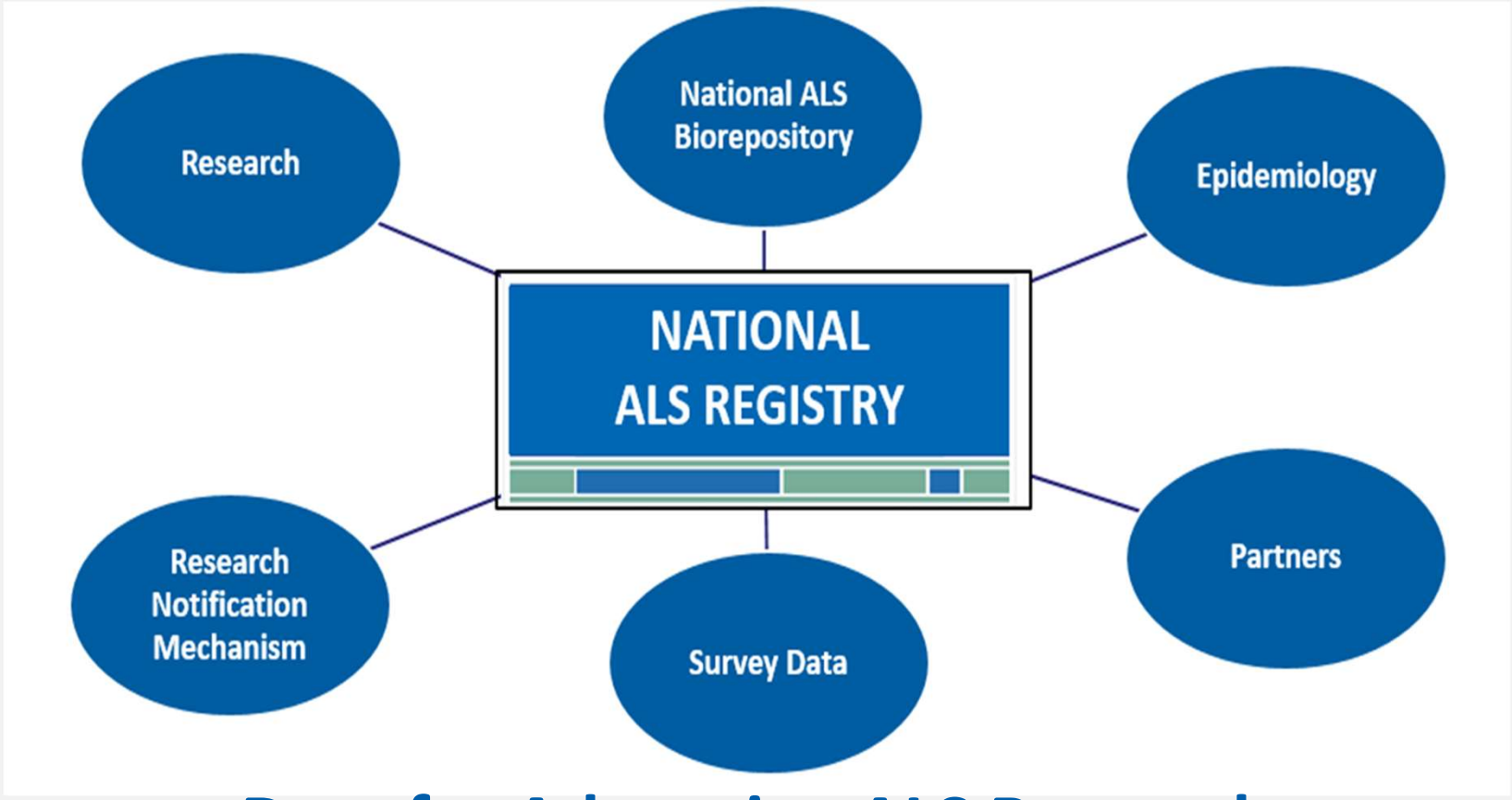
Paul Mehta

Principal Investigator

National ALS Registry

Centers for Disease Control and Prevention

National ALS Registry Overview



Data for Advancing ALS Research

Neil Thakur

Chief Mission Officer

The ALS Association

Carolina Mendoza-Puccini

Program Officer, Division of Clinical Research

National Institute of Neurological Disorders and Stroke

National Institutes of Health

NINDS Common Data Elements Project

Carolina Mendoza-Puccini, MD (She/Her)
Carolina.Mendoza-Puccini@nih.gov

National Institute of Neurological Disorders and Stroke

NINDS Common Data Elements
Harmonizing information. Streamlining research.

NINDS CDE Project

- A repository of validated instruments
- Readily available Case Report Forms (CRFs) for documentation
- Readily available data dictionaries to be uploaded into electronic data capture systems
- Open-Access for the scientific community (NIH and non-NIH funded)

Use of CDEs at NINDS

For NINDS grants:

- Phase 2-3 Trials, Epi studies
- Built into NoA milestones

Funding Opportunities

NIH
NLM
ODSS

ALS Data

- CReATe
- dbGaP
- NINDS Archived Clinical Research Datasets

NIH Data Sharing Policy (2003)

- Final research data
- $500,000 or more in DC in any year of the proposed project period
- Funding Institute additional requirements

New DS Policy (eff. Jan 2023)

- Data management and sharing plan
- NIH IC additional requirements

www.commondataelements.ninds.nih.gov

Session 3 | Discussion Questions

1. What are the barriers to data sharing in clinical research for ALS and how can research consortiums and funders facilitate open data exchange?

2. How can researchers and trialists maximize the interoperability of data collected as part of preclinical studies and clinical trials for ALS?

3. How can data sharing policies for federally funded research maximize the scientific value of clinical data collected as part of ALS trials?

4. What other mechanisms are needed to increase effective collaboration and minimize competition in ALS research?

Session 4: Understanding What is Meaningful for Patients - Recruitment, Patient Experience Data, and Expanded Access

1:05pm – 2:05pm

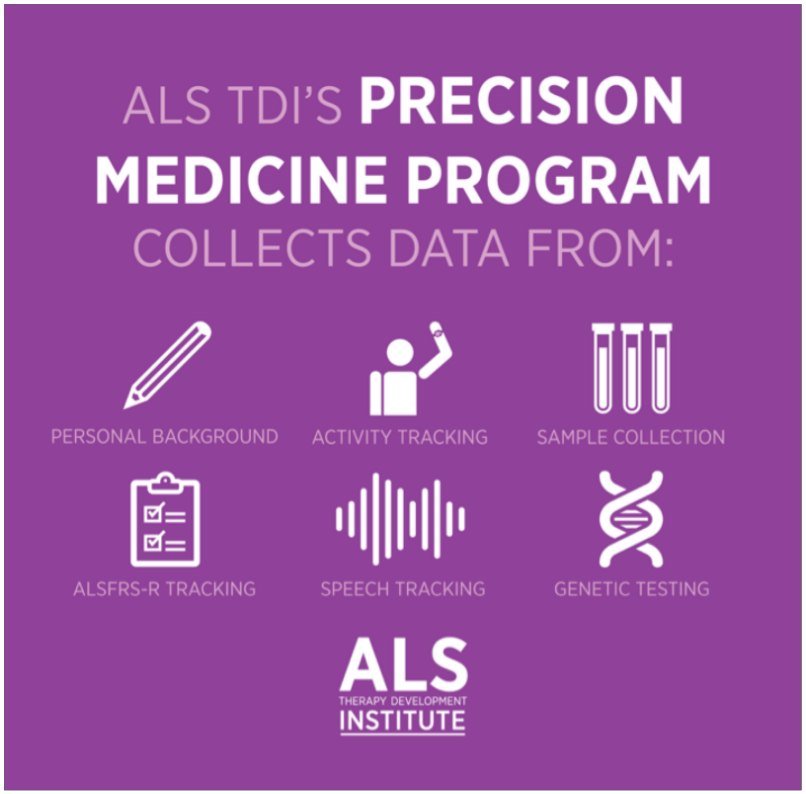
Fernando Vieira

Chief Scientific Officer

ALS Therapy Development Institute

Understanding What is Meaningful to pALS

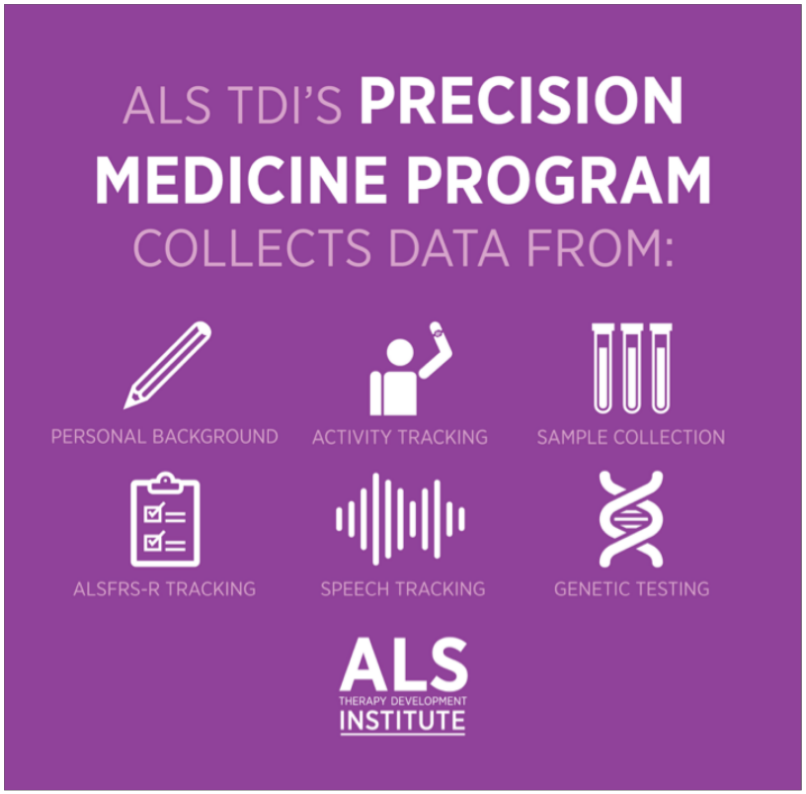
Understanding What is Meaningful to pALS



Our personal background surveys explore four broad domains:

- Lifestyle
- Medical History
- Occupation
- Participants' experiences with ALS

Understanding What is Meaningful to pALS



Key learnings regarding what is meaningful for patients:

- Cast a wide net to collect information.
- Participants appreciate participating from home.
- Participants appreciate access to their data.
- Participants are motivated by interaction with people who interface with their data.

Sandy Morris

ALS Patient Advocate

I AM ALS

Developing the PaCTD Rating System

- I AM ALS Clinical Trials Team created the Patient-Centric Trial Design (PaCTD) Rating System.
- Overarching Goal:
    - Partnership between patient and sponsor to create humane & efficient trials that will increase ROI. Key elements include:
        - Patient-centricity in design
        - Align with the FDA's 2019 *Amyotrophic Lateral Sclerosis: Developing Drugs for Treatment Guidance for Industry*.

The PaCTD Criteria

1. Optimizes access to investigational therapies (60%). This category addresses whether a trial includes:
    - Open-Label Extension
    - Minimal placebo usage
    - An Expanded Access Program
2. Advances scientific progress (30%). This category addresses whether a trial includes the following elements:
    - Consideration of disease heterogeneity
    - Use of scientifically-justified eligibility criteria
    - Investigation of one or multiple biomarkers
    - Independent unblinded review panel
3. Is patient friendly (10%). This category addresses whether a trial includes the following elements:
    - Use of run-in observation period
    - Reduces travel burden by use of novel methods

Weighting of the Nine Trial Elements

- Prioritization matrix
  - Twelve members participated in the exercise to determine priority of the nine criteria using the prioritization matrix.
- Method
  - Criteria #1 was compared to Criteria #2, asking the question, "Is Criteria #1 of more, equal, or lesser value than Criteria #2?"
  - A score of “10" was given if the evaluator thought that Criteria #1 was "much more value" than #2.
  - A score of “5" was given for "more value" and a score of “1" for "equal value."
  - If the criteria was deemed "less value" a score "0.2" was given and for "much less value" a score “0.1" was given.
  - This process continued by comparing Criteria #1 to each subsequent criteria items 2-9 on the clinical trial ratings priority list.
  - This process was replicated for each subsequent criteria element down the list.
  - The results from all twelve participants were aggregated into the final priority list based on score. And informed how much weight should be allocated to each criteria.

The PaCTD Ratings

PaCTD Rating* ▼	Drug/ Treatment	Sponsor	Country	Recruitment Status	E
★★★★★	Zilucoplan (...	MGH	USA	Recruiting	
★★★★★	Verdiperstat ...	MGH	USA	Recruiting	
★★★★★	CNM-Au8 (H...	MGH	USA	Recruiting	
★★★★	BIIB067 (Tof...	Biogen	USA, Australi...	Recruiting	
★★★★	Arimoclomol	Orphazyme	USA, Belgiu...	Not Recruiting	
★★★★	Ravulizumab...	Alexion Ph...	USA, Canada...	Recruiting	
★	NurOwn	Brainstorm ...	USA	Not Recruiting	

Paul Melmeyer

Director of Regulatory Affairs

Muscular Dystrophy Association

Kristina Bowyer

Vice President

Patient Centric Drug Development

Ionis

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to **science,**
to **medicine**
and to **patients**

January 28, 2021

Kristina Bowyer,

VP Patient Centric Drug Development

Cytokinetics

Biogen

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impact ALS

INVESTIGATING AND MEASURING PATIENT AND CAREGIVER TRENDS ABOUT ALS

ALS ASSOCIATION

rmn Research Motor Neurone

impact ALS EUROPE

The Voice of the Patient

Summary report resulting from an externally conducted Patient-Focused Drug Development survey, a parallel effort to the U.S. Food and Drug Administration's Patient-Focused Drug Development Initiative

Amyotrophic Lateral Sclerosis (ALS)

ALS Patient-Focused Drug Development Survey
October – November 2017

Conducted by: The ALS Association
Version Date: October 24, 2019

ALS ASSOCIATION

Submitted as patient experience data for consideration pursuant to section 569C of the Federal Food, Drug, and Cosmetic Act to:
Center for Drug Evaluation and Research (CDER) &
Center for Biologics Evaluation and Research (CBER)
U.S. Food and Drug Administration

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Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, 2020; 0: 1–9

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ORIGINAL ARTICLE

Understanding the needs of people with ALS: a national survey of patients and caregivers

KATE T. BRIZZI[1,2], JOHN F. P. BRIDGES[3], JILL YERSAK[4], CALANEET BALAS[4], NEIL THAKUR[4], MIRIAM GALVIN[5], ORLA HARDIMAN[5], CHAD HEATWOLE[6], JOHN RAVITS[7], ZACHARY SIMMONS[8], LUCIE BRUIJN[9], JAMES CHAN[10], RICHARD BEDLACK[11] & JAMES D. BERRY[1]

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Abstract

Objective: Amyotrophic lateral sclerosis (ALS) has profound effects on people with ALS (PALS) and caregivers. There is a paucity of research detailing and comparing PALS and caregiver day-to-day perspectives of ALS. *Methods:* A survey developed collaboratively by The ALS Association and a panel of experts in ALS care was designed to broadly sample the experience of PALS and caregivers with respect to physical and emotional symptoms, the efficacy of treatment approaches, and goals for future treatments. Specific physical symptoms assessed consisted of fatigue, pain, weakness, shortness of breath, difficulty sleeping, speech problems, depression and other mood changes, and cognitive changes. PALS, caregivers of living patients with ALS (C-LPALS), and caregivers of deceased patients with ALS (C-DPALS) were contacted by email to participate in a 30-minute online survey. *Results:* 887 PALS, 444 C-LPALS, and 193 C-DPALS responded to the survey. In comparison to PALS, C-LPALS perceived that PALS had significantly higher rates of all surveyed symptoms except for pain and weakness. Caregivers self-reported higher stress levels than PALS ($p < 0.001$). 35% (135/383) of caregivers reported experiencing a devastating or near devastating financial impact of ALS and 64% (247/383) of caregivers felt their own health had worsened. Caregivers were significantly less likely to perceive a positive response to treatment in comparison to PALS ($p < 0.001$). *Conclusions:* PALS and caregivers report a number of symptoms beyond weakness that affect daily life which may be targets of future interventions. There are opportunities to improve services and care for caregivers to reduce the burden of illness.

Keywords: Therapy, epidemiology, dementia, ALS, caregiven, quality of life, patient-reported outcome measures

Introduction

Amyotrophic lateral sclerosis (ALS) has wide-reaching effects on patients and caregivers. Symptom and function-based ALS outcome measures, such as the Revised ALS Functional Rating Scale (ALSFRS-R) (1), the CNS-Lability Scale (CNS-LS) (2,3), the Patient Health Questionnaire-9 (4), and pulmonary function tests help quantify the severity of a select set of ALS symptoms and overall patient function; however, these scales and metrics lack the ability to report the ALS patient's overall experience in many symptomatic areas. Direct input from the patient is important in understanding the disease

Supplemental data for this article is available online at https://doi.org/10.1080/21678421.2020.1763089

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DOI: 10.1080/21678421.2020.1763089

PEOPLE LIVING WITH ALS AND THEIR CAREGIVERS' INPUT INTO DRUG DEVELOPMENT IN EUROPE

impact ALS EUROPE

M Galvin[1], O Hardiman[1,2], M Heverin[1], C McDermott[3], B Charpentier[4], K Stenson[5], K Bowyer [6]

[1]Academic Unit of Neurology, Trinity College Dublin, Ireland, [2] Beaumont Hospital, Dublin, Ireland [3] University of Sheffield, UK [4]Cytokinetics, South San Francisco, USA, [5]Biogen, Cambridge, MA, USA,[6] Ionis, Carlsbad, CA, USA

Introduction

There is an emerging focus on patient and caregiver engagement in the determination of clinically meaningful outcomes, and for input to key areas of drug development.

The IMPACT European survey of people with amyotrophic lateral sclerosis (ALS) and caregivers is gathering data on the overall burden of disease, psychological distress and the loss of function over the course of the disease.

Objective

To survey ALS patients and caregivers across 9 countries in Europe – UK, Ireland, Germany, France, Spain, Italy, Belgium, Netherlands, Sweden

Findings from the European survey will be viewed in comparison with results from a similar 2017 US survey.

Methods

- The survey questions were used in a previous US survey[1] and adapted for European contexts.
- Recruitment of people with ALS and caregivers (current, former and bereaved) was carried out in each of the participating countries with the partnership of European Network for the Cure of ALS (ENCALS) and advocacy groups in each country.
- GDPR compliant anonymous on-line surveys open from October 2020 with a planned closing date for December 2020.
- Preliminary data are discussed in this presentation
- Ethical approval for this study was received from Trinity College Dublin.

Patient Survey
- Module 1: ALS Diagnosis and Care
- Module 2: Living with ALS
- Module 3: Approaches to Treating ALS
- Module 4: Background Demographics

Caregiver Survey
- Module 1: ALS Diagnosis and Care
- Module 2: Living with ALS
- Module 3: Approaches to Treating ALS
- Module 4: Background Demographics
- Module 5: Background and Burden as a Caregiver

Results PRELIMINARY DATA*

* Preliminary Data as on 29th October 2020

FIGURE 1: RESPONDENTS BY SEX

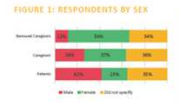
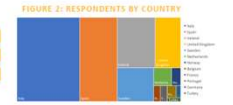


FIGURE 2: RESPONDENTS BY COUNTRY



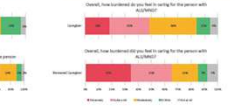
Patients (N=206) Caregivers (N=110) Bereaved Caregivers (N=83) Total (N=399)

TABLE 1: IN WHICH COUNTRY DO YOU LIVE?

	Patients (N=206)		Caregivers (N=110)		Bereaved Caregivers (N=83)		Total (N=399)	
Country	n	%	n	%	n	%	n	%
Did not specify	73	35%	40	36%	28	34%	141	35%
Italy	65	31%	26	25%	8	10%	99	25%
Spain	17	8%	15	14%	27	33%	59	15%
Ireland	17	8%	13	12%	6	7%	36	9%
United Kingdom	17	8%	4	4%	3	4%	24	6%
Sweden	10	5%	5	5%	8	10%	23	6%
Netherlands	3	1%	2	2%	3	1%	8	2%
Norway	3	1%	0	0%	0	0%	3	1%
Belgium	1	0%	1	1%	0	0%	2	1%
France	0	0%	0	0%	2	2%	2	1%
Portugal	1	0%	1	1%	0	0%	2	1%
Germany	0	0%	1	1%	0	0%	1	0%

FIGURES 3A&B: CAREGIVER STRESS

FIGURES 4A&B: CAREGIVER BURDEN



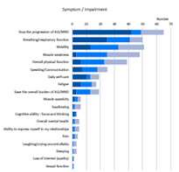
Discussion and Conclusion

The IMPACT European surveys will be open for completion through to December 2020. There is ongoing monitoring of the national-response numbers and cooperation with local advocacy groups to maintain and encourage participation.

The preliminary data suggest a positive uptake of the surveys and a welcome opportunity to present the voices of patients and caregivers. On survey completion, the analyses of the complete data sets will provide information on issues such as the prevalence of genetic testing, disease symptoms that would preferably be treated, participation in clinical trials and quality of life issues for both people with ALS and their caregivers.

This study provides important information on the burden of disease from the perspectives of people living with ALS and those caring for them in many countries in Europe; this will help to better understand clinical pathways, moments of impact and clinical meaningfulness.

FIGURE 5: WHICH SYMPTOM / FUNCTIONAL IMPAIRMENT DO PATIENTS MOST WANT TREATMENT TO BENEFICIALLY IMPACT?



Acknowledgements: People with ALS and their caregivers, The IMPACT European Survey Advisory Group.

Funding provided by Cytokinetics, South San Francisco, USA; Biogen, Cambridge, MA, USA; Ionis, Carlsbad, CA, USA.

To watch presentation please click here

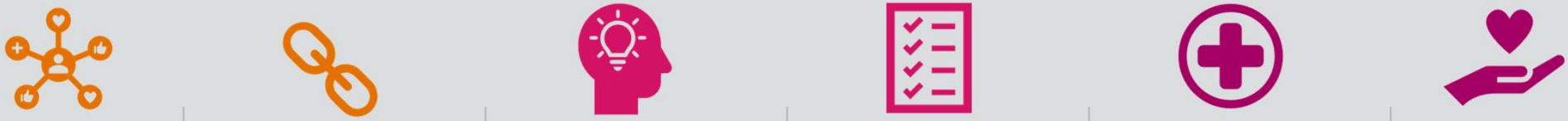
Cytokinetics Biogen IONIS TRINITY COLLEGE DUBLIN rmn

Patient Insights Drive More Effective, Efficient Trials

1. Discovery | **2. Development** | **3. Delivery**

Idea — Basic Research — Clinical Trials — Regulatory Approval — Access to Treatments

Clinical trials have greater chance of success through:



- Understand Patient Needs
- Interconnect Science and the Need
- Improved Study Design
- Meaningful Clinical Endpoints
- Important Patient Benefits
- Patient Wellness & Quality of Life

IONIS


thank you
hope

Julia Tierney

Chief of Staff

Center for Biologics Evaluation and Research

U.S. Food and Drug Administration

Session 4 | Discussion Questions

1. How can researchers better engage patients in the design of clinical trials?

2. How do researchers balance the needs of a trial while minimizing the burden on patients?

3. What are the barriers to the development and validation of novel endpoints that correlate to clinically meaningful benefits for ALS patients?

4. How can qualitative research contribute to improved patient-informed endpoint development?

5. What role can digital tools play in complimenting data collected thought traditional clinical outcome assessments, including patient-reported outcomes (PROs)? How can patients and their caregivers play a role in collecting patient experience data that can inform ALS drug development?

6. What are the key considerations for the development and implementation of expanded access programs that allow access to therapeutics outside of traditional clinical trials?

Session 5: Coordination, Collaboration, and Shared Strategy

2:15pm – 3:25pm

Merit Cudkowicz

Chief of the Neurology Service

Director, Sean M. Healey & AMG Center for ALS

Massachusetts General Hospital

Toby Ferguson

Head of the Neuromuscular Development Unit

Biogen

Bryan Traynor

Neurologist & Senior Investigator

National Institute on Aging

National Institutes of Health

Richard White

Policy Analyst

National Organization for Rare Diseases

Wilson Bryan

Director

Office of Cellular, Tissue, and Gene Therapies

U.S. Food and Drug Administration

Eric Bastings

Deputy Director, Office of Neuroscience

Acting Director, Division of Neurology 1, Office of Neuroscience

U.S. Food and Drug Administration

Session 5 | Discussion Questions

1. What are the next steps to accelerate ALS drug development? How do you envision the role of patient, industry, research, and regulatory stakeholder groups in advancing drug development?

2. To what extent is ALS research siloed and/or unnecessarily duplicative? If this is a problem, how can it be addressed?

Closing Remarks & Meeting Adjournment

Mark McClellan, MD, PhD

Director, Duke-Margolis Center for Health Policy

Thank You!

Contact Us

healthpolicy.duke.edu

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