



22nd Annual SMA Researcher Meeting

Thursday June 14, 2018

8:30 AM Welcoming Remarks
Jill Jarecki PhD, Cure SMA Chief Scientific Officer

Special Session: Clinical and Basic Questions of SMA in the Era of SMN Repletion: Challenge and Opportunity, Moderator, Richard Finkel MD, Chief, Division of Neurology, Nemours Children's Hospital

The advent of an FDA approved SMN enhancing drug has ushered in a new stage in the SMA community. As we celebrate the long awaited first drug approval, we know there remains much to be done. While Spinraza offers tremendous benefit to those with SMA, there is also a need for continued research. The development of additional therapies to be used independently or in combination with SMN enhancing approaches requires understanding more about SMA biology and disease mechanisms. Studying the "new" SMA phenotype after treatment will unveil new, unmet patient need, perhaps including extra-neuronal phenotypes and the need for such therapies. The goal of this session is to discuss these new challenges and opportunities. The session begins by exploring the efficacy and unmet needs of current treatment and is followed by investigating patient phenotypes post treatment. Next, the neurodevelopmental need for prenatal SMN is discussed and its requirement for complete restoration of phenotype. Following that will be a discussion of the unanswered basic biology questions pertaining to SMA and their implications for therapy development. The panel discussion will focus on prioritizing future research endeavors to address unmet medical need for SMA patients.

8:35 AM Introduction to the Special Session
Richard Finkel MD, Chief, Division of Neurology, Nemours Children's Hospital

8:40 AM Exploring Unmet Medical Need in SMA: Comparing SMN Enhancing Efficacy in Pre-symptomatically Versus Symptomatically Treated Patients
Thomas Crawford MD, Professor of Neurology and Pediatrics, Johns Hopkins School of Medicine

9:05 AM Unmet Medical Need in Adults and Teens with SMA
John Day MD, PhD, Professor, Neurology & Neurological Sciences Director, Stanford Neuromuscular Disorders Program, Stanford University Medical Center

9:30 AM Overview of Therapies in Development: What are the Current Gaps in the SMA Drug Pipeline?
Stephen Kolb MD, PhD, Associate Professor, Department of Neurology and Department of Molecular & Cellular Biochemistry, Ohio State University

9:55 AM Extra-neural and Peripheral Phenotypes of SMA
Basil Darras MD, Professor of Neurology, Harvard Medical School

Break

10:45 AM Is there a Developmental Component to SMA: Is SMN Required Prenatally?
Charlotte Sumner MD, Professor of Neurology, Johns Hopkins School of Medicine

11:10 AM SMA Biology: What We Know and What We Need to Know in Our Understanding of SMA?
Arthur Burghes PhD, Professor of Molecular and Cellular Biochemistry, Ohio State University

11:35 AM The Role of SMN at the NMJ: Current Knowledge and Remaining Questions.
Umrao Monani PhD, Associate Professor of Pathology and Cell Biology, Columbia University

12:00 PM Closing Remarks and Panel Discussion
Moderated by Richard Finkel MD

12:30 PM Lunch

12:30 PM Biogen Symposium

Modifiers of Disease and Therapeutic Targets

Session Moderator: Elliot Androphy MD

2:00 PM Brunhilde Wirth: CHP1 Reduction Ameliorates Spinal Muscular Atrophy Pathology by Restoring Calcineurin Activity and Endocytosis

2:20 PM Eric Villalon: Stmn1 Overexpression Ameliorates Phenotype in an Intermediate Mouse Model of Spinal Muscular Atrophy

2:40 PM Meaghan Van Alstyne: Dysregulation of Mdm2 and Mdm4 Alternative Splicing Underlies p53 Anti-Repression and Motor Neuron Degeneration in Spinal Muscular Atrophy

3:00 PM Sibylle Jablonka: Calcium Channel Modulation Ameliorates Morphological and Functional Abnormalities of Motoneurons in Mouse Models for Spinal Muscular Atrophy

3:20 PM Remy Bordonne: Characterization of the Protective Mechanism of the Acp1 Modifier in SMN-Deficient Fission Yeast Cells

- 3:40 PM Allison Ebert: Aberrant GATA6 Expression Induces Senescent-Like Phenotypes in iPSC-Derived Astrocytes
- 4:00 PM Katharina Meijboom: Using CMAP for the Development of Second Generation Therapies for SMA: Harmine Shows Promising Effects In Vivo and In Vitro
- 4:30 PM Poster Session A and Cocktail Reception
Odd Numbered Posters**
- 6:30 PM Meet and Greet and Annual Relay Race with SMA Families**

Friday June 15

7:00 AM Genentech/Roche Symposium

SMN Function and Expression

Session Moderator: Adrian Krainer, PhD

- 8:30 AM Corey Ruhno: Identification of Deletion Junctions and Variants that Affect Genotype-Phenotype Prediction in Spinal Muscular Atrophy
- 8:50 AM Alberto Kornblihtt: Intragenic Histone Acetylation Enhances Upregulation of SMN2 Exon 7 Inclusion by Antisense Oligonucleotides
- 9:10 AM Audrey Winkelsas: Targeting the 5'UTR of SMN2 as a Combinatorial Therapeutic
- 9:30 AM Oliver Gruss: Identification of Cellular Signaling Cues Regulating the SMN Complex and its Implications for SMA
- 9:50 AM Eric Ottesen: High-affinity RNA Targets of the Survival Motor Neuron Protein Reveal Diverse Preferences for Sequence and Structural Motifs

Break

SMA Pathology and Tissue Requirements

Session Moderator: Rashmi Kothary, PhD

- 10:40 AM Marc-Oliver Deguise: Abnormal Fatty Acid Metabolism is a Feature of Spinal Muscular Atrophy
- 11:00 AM George Mentis: Complement and Microglia Mediate Sensory-Motor Synaptic Loss in Spinal Muscular Atrophy
- 11:20 AM Lingling Kong: Impaired Motor Axon Radial Sorting and Growth is Followed by a Rapid Phase of Axonal Degeneration in Severe SMA

11:40 AM Basil Darras & Thomas Crawford: Phosphorylated Neurofilament Heavy Chain (pNF-H) as a Potential Biomarker of SMA disease Activity: pNF-H Levels at Baseline and During Treatment in the Nusinersen Clinical Trial Program

12:00 PM Boxed Lunch

**12:30 PM Poster Session B
Even Numbered Posters**

**Clinical Research Studies for SMA
Session Moderator: Tom Crawford, MD**

2:20 PM Francis Lee: Newborn Screening for Spinal Muscular Atrophy in the US

2:40 PM Kathryn Swoboda: Utilization of the Newborn Screening Translational Research Network (NBSTRN): Project Cure SMA Longitudinal Pediatric Data Repository (LPDR)

3:00 PM Jacqueline Glascock: Treatment Algorithm for Infants Diagnosed with Spinal Muscular Atrophy through Newborn Screening

3:20 PM Mary Schroth: SMA Clinical Care Center Network and SMA Clinical Data Registry

3:40 PM Amy Pasternak: Caregiver Reported Motor Performance is Associated with Motor Capacity in Children and Young Adults with Spinal Muscular Atrophy (SMA)

4:00 PM Ashley Goodwin: Performance of the Six Minute Walk Test in Pediatric Neuromuscular Disease: Review and Comparison to Healthy Population Normative Values for use in Spinal Muscular Atrophy

4:20 PM Sally Dunaway Young: Scoliosis is Negatively Associated with Motor Function in Children with Later-Onset SMA

4:40 PM Grazia Zuppa: Cognitive Development (IQ), Language Comprehension and Motor Functioning in SMA1 Children using AAC

6:30 PM Evening Activity: Family Friendly Poster Sessions with SMA Families

Saturday June 16

Morning Podium Sessions (8:30 AM to 12:00 PM):

7:00 AM AveXis Symposium

**8:30 AM Podium Poster Highlights
Session Moderator: Samuel Pfaff, PhD
Poster presentations are selected by the Cure SMA SAB for five-minute presentations**

Preclinical and Clinical Drug Development

- 9:20 AM Bakri Elsheikh: The Ohio State University Wexner Medical Center (OSUWMC) Experience in Treating Adults with Spinal Muscular Atrophy with Nusinersen
- 9:40 AM Jacqueline Montes: Ambulatory Function and Fatigue in Nusinersen-Treated Children with Spinal Muscular Atrophy
- 10:00 AM Michelle Farrar: Longer-term Assessment of the Safety and Efficacy of Nusinersen for the Treatment of Infantile-onset Spinal Muscular Atrophy (SMA): An Interim Analysis of the SHINE Study
- 10:20 AM Darryl De Vivo: Nusinersen in Infants Who Initiate Treatment in a Presymptomatic Stage of SMA: Interim Efficacy and Safety Results from the Phase 2 NURTURE Study
- 10:40 AM John Day: Update of CY 5021: A Phase 2 Clinical Trial of Reldesemtiv, a Fast Skeletal Muscle Troponin Activator (FSTA), for the Potential Treatment of Spinal Muscular Atrophy
- 11:00 AM Richard Shell: AVXS-101 Phase 1 Gene Therapy Clinical Trial in SMA Type 1: Improvements in Respiratory and Bulbar Function Leads to Fewer and Less Lengthy Hospitalizations Compared to Natural History
- 11:20 AM Ksenija Gorni: Updated Pharmacodynamic and Safety Data from SUNFISH Part 1, a Study Evaluating the Investigational Oral SMN2 Splicing Modifier RG7916 in Patients with Type 2 or 3 Spinal Muscular Atrophy
- 11:40 AM Giovanni Baranello: RG7916 Significantly Increases SMN protein in SMA Type 1 Babies
- 12:00 PM Enrico Bertini: A Long-Term, Open-Label, Follow-Up Study of Olesoxime in Patients with Type 2 or Non-Ambulatory Type 3 Spinal Muscular Atrophy who Participated in a Placebo-Controlled Phase 2 Trial
- 12:20 PM Closing Remarks**
Jacqueline Glascock, PhD, Senior Scientific Program Manager, Cure SMA

Meeting Adjourns