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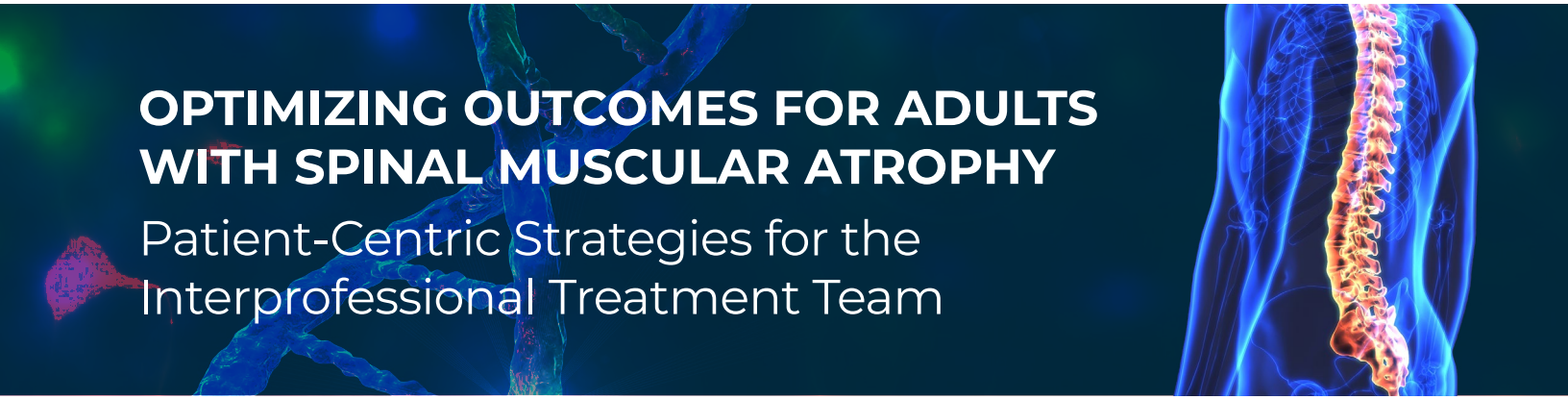

OPTIMIZING OUTCOMES FOR ADULTS WITH SPINAL MUSCULAR ATROPHY

Patient-Centric Strategies for the Interprofessional Treatment Team

- Spinal muscular atrophy (SMA), categorized into types 0 through 4, describes a group of rare genetic disorders that causes loss of spinal α-motor neurons, leading to muscle weakness and atrophy; over 95% of cases are an autosomal recessive disorder from deletion or mutation of the survival of motor neuron (SMN1) gene
  - While SMA typically presents in childhood, 25% of those living with SMA are adults, and these adults face unique and underrecognized challenges with mental health and independent living
- The relatively recent introduction of disease modifying therapy (DMT) in SMA altered the treatment paradigm of a disease historically managed only with supportive care; there are 2 DMTs FDA-approved for use in adults, nusinersen and risdiplam
- Nusinersen is an intrathecally-administered survival motor neuron-2 (SMN2)-directed antisense oligonucleotide; thus far, benefit of nusinersen in adults with SMA is largely based on observational study:
  - A prospective observational cohort study looked at 139 patients with SMA aged 16 – 65 years who received nusinersen for minimum treatment of 6 months, to a follow-up of up to 14 months; patients receiving nusinersen had a clinically meaningful improvement in baseline motor function as measured by the Hammersmith Functional Motor Scale Expanded (HFMSE) score, assessed at months 6, 10, and 14 (28% of participants achieved a 3-point or higher increase in HFMSE at 6 months, 35% at 10 months, and 40% at 14 months)
  - A retrospective cohort study looked at 116 patients aged 18-72 with later-onset SMA, types 2 and 3, and found meaningful median change from baseline in HFMSE scores (1 at 6 months, 2 at 10 months, and 3 at 14 months), Revised Upper Limb Module (RULM) scores (0 at 6 months, 1 at 10 months, and 2 at 14 months), and 6-Minute Walk Test (6MWT) score (11 at 6 months, 25 at 10 months, and 20 at 14 months)
- Risdiplam is an orally administered survival of motor neuron 2 (SMN2) splicing modifier; in the randomized, placebo-controlled SUNFISH trial of 231 participants aged 2 to 25 years of age, risdiplam was the first treatment to have pivotal placebo-controlled data in a broad population of patients with SMA, and the ongoing open-label JEWELFISH study (NCT03032172) will look at risdiplam safety and include older patients previously treated with other medications
  - In SUNFISH, Motor Function Measure 32 (MFM-32) and RULM scores increased by 1.36 and 1.61 for participants in the risdiplam group, as compared to those not taking risdiplam, who showed an average score decrease of 0.19 and increase of 0.02, respectively
- Adults with SMA experience a significant amount of depression, anxiety, and difficulty in everyday activities of independent living; these issues have inspired a **Call to Action** aimed at empowering patients with SMA while improving care, health outcomes, and quality of life:

Long-term Aspirations and Calls to Action

Provide Age-appropriate and Comprehensive Care That Delivers the Most Meaningful Health Outcomes and QoL for Adults Living with SMA	• Conducting more longitudinal studies in the treatment era that enable better prediction of the multifaceted challenges faced by adults and clinical/real-world studies that can evaluate benefits of supportive care (e.g., exercise, rehabilitation) • Evolving assessment frameworks to better reflect adult (and disease) circumstances (e.g., age-appropriate tests according to disease severity), to be more sensitive to clinical outcomes most meaningful to adults (e.g., mobility, pain, mental health) and to align with patient-reported quality of life outcomes (e.g., autonomy, well-being) • Capacity-building through education, training, and sharing of best practices and facility adaptation to ensure adults receive appropriate care
Establish More Integrated Pathways That Enable Adults Living with SMA to Optimally Manage Their Multifaceted Healthcare Needs	• Advocating for policies that lead to more coordinated approaches to care (e.g., through single-site clinics, dedicated care managers as points of contact) • Integrating best practices and dedicated processes (e.g., formal transitional care clinics, communication pathways between pediatric and adult specialists, national network of specialists) that facilitate the transition to adult care and knowledge transfer • Integrating value-adding digital tools that allow patients to (re-)engage and/or (re-) integrate into the health system
Strengthen Social and Financial Support Systems That Empower Adults Living with SMA and Their Caregivers to Fulfill Their Personal Goals	• Enhancing social services that are easily navigated and accessed by adults and accessibility policies that can impact the lives of those with SMA (and others with disabilities) • Promoting patient-driven community networks to share knowledge and best practices, discuss experiences, empower the patient and caregiver voice, and provide support for adults living with SMA via online portals and books/ pamphlets on pressing topics (e.g., raising children, sexual health) • Assessing the socioeconomic implications of SMA on caregivers to provide an evidence-informed proposal for decision makers around funding and support • Evaluating financial support structures that account for the patient and community voice, and identifying evidence-based options that are positioned to empower adults living with SMA and their caregivers to accomplish their personal goals

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