Medical Management of Adults with SMA

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The workshop will address several questions.

1) Who represent the adult SMA population?

Spinal muscular atrophy (SMA) is an autosomal recessive inherited neuromuscular disorder, caused by a mutation in the survival motor neuron *(SMN)* gene, characterized by loss of spinal motor neurons leading to diffuse muscle weakness and atrophy. The disorder usually begins in infancy or childhood. Most adults with the disease represent the so-called type 2 patients, defined by the fact that they obtained the ability to sit, but never walked alone. Type 3 disease patient are defined as those who walked independently at some point in the lives. In addition, a small group of SMA patients does not become symptomatic until after age 18 years and are referred to as type 4 patients.

We will delineate the differences between the phenotypes in the adult population as well as the impact of that on the overall prognosis.

2) The relevance of SMA genetics to the adult population?

SMA is caused by the SMN protein deficiency. There are normally two copies of the *SMN* gene, the gene involved in SMA, on each chromosome; the primary gene copy (called *SMN1*), and an almost identical copy, *SMN2*. *SMN2* produces the same protein as does *SMN1*, but produces only about 10% of normal, full-length mRNA expression because of aberrant splicing of most of its message. Loss of both copies of the *SMN1* occurs in 96% of SMA, and is the cause of the disease. In the greater number of patients, the deletion is inherited from the parents. Rarely, a de-novo deletion in one of the two alleles can occur. In 3-4%, other mutations in *SMN1* gene can be found in one allele associated with deletion in the other one.

The severity of the disease, however, is primarily related to the number of SMN2 copies, which serves a somewhat protective function against the loss of SMN1, since SMN2 can partially compensate for SMN1. We will also discuss the role of other genetic modifiers.

3) **What does the Standards of Care (SOC) document tells us about management of the adult population?**

We will address the benefits of multidisciplinary team approach with specific attention to the importance of integrating, coordinating, and directing one's own care.

Several aspects of the standard of care will be discussed including clinical assessment and rehabilitation needs based on functional status (Sitters versus walkers). Specifics on stretching techniques, positioning, mobility and exercise as well as chest physiotherapy will be discussed. The workshop will also address management of spinal and chest deformity as well as contractures. Furthermore, we will discuss bone health in the adult population as well as nutrition, swallowing and gastrointestinal dysfunction management. Additionally, we will discuss pulmonary management and acute-care issues as well as immunization and role of supplements.

We will also cover other care-related subjects such as pain, depression and anxiety management.

4) **What is the current experience regarding use of Spinraza in adults with SMA?**

The workshop will address the challenges to obtaining Spinraza approved by insurance companies, the alternative programs that may allow for access to the treatment, options for intrathecal delivery of the drug in subjects with spinal fusion as well; we will share the experience from and preliminary data on the safety and preliminary efficacy of treatment in the adult population.

5) **What is in the pipeline for the Adult SMA population?**

We will discuss the latest research in SMA and relevance to the adult- SMA population as well as rational combination therapies that may be considered in adults with SMA.

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