Clinical Challenges of Providing Nusinersen for Spinal Muscular Atrophy and the Implications for Newborn Screening

Jennifer Kwon, MD
University of Rochester Medical Center
Rochester, NY
Disclosures (who am I?)

- **Sanofi-Genzyme**-site PI, Genzyme Registry; travel
- **Biomarin** – consultant fees, travel
- Evidence Review Group (Kemper, PI)

*My comments are my own should not be taken to reflect the views of any federally sponsored agency, including the ERG*
Objectives

• Explain why nusinersen (Spinraza®) is such an exciting treatment for spinal muscular atrophy (SMA)

• Discuss the barriers to effective and efficient delivery of nusinersen
Spinal Muscular Atrophy

Motor Neuron Death

Corresponding Muscle Wasting
SMN2 gene

Transcription
Pre-mRNA splicing
Translation

ISS-N1
GUAAGUCUGCCAGCAUUUAUGAAAGUGAAUCUU
Spinraza™ (nusinersen)

SMNΔ7
Less stable and partially functional protein

SMN
Highly stable and fully functional protein
4 weeks Parents noted weakness
7 weeks Diagnosed with SMA

7 weeks Started receiving ISIS SMN$_{RX}$

Google: Cameron SMA nusinersen
Antisense oligonucleotide solution injected into the intrathecal space (into the spinal fluid)
9 months reaching with sustained play
One difference between these boys...ISIS SMNrx

B
- Low muscle tone at 2 months old
- Diagnosed at 4 months old
- Permanent ventilation at 5 months old after his first cold.
- Cannot sit up, swallow or move

C
- Lost all movement at 5 weeks old.
- Diagnosed at 1 month old
- Began SMNrx at 7 weeks old.
- Can sit unassisted and stand
Timeline

• 2015-2016  ISIS SMN_{RX} results
• December 2016  FDA approved nusinersen (Spinraza) for SMA , “all types, all ages”
• Announced the price: $750,000 in the first year, and $375,000 annually for life.
Barriers

• High cost

• Managing the needs of SMA patients of “all ages and all types”
US Hospital Business 101

Part I. Expensive Drugs

– Given in an outpatient setting
– Are never fully reimbursed by Medicaid
– Are financially risky to store in hospital pharmacies
– Are likely to cause deficits in pharmacy budgets because of the lag in payments
Challenges of Intrathecal Administration

• In modern hospitals, places to performing lumbar punctures (LPs) are limited
• The location of this procedure depends on whether sedation is required or not
• Issues of scheduling rooms and personnel over two months
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Every 4 months after that
Work in Progress

• Ideally, centers would have a certain volume SMA patients to justify the resources needed
• A reasonable business plan for treating SMA longterm with nusinersen is unlikely to be equitable or just
It’s Complicated