

# Personalizing the Treatment Approach in ALS

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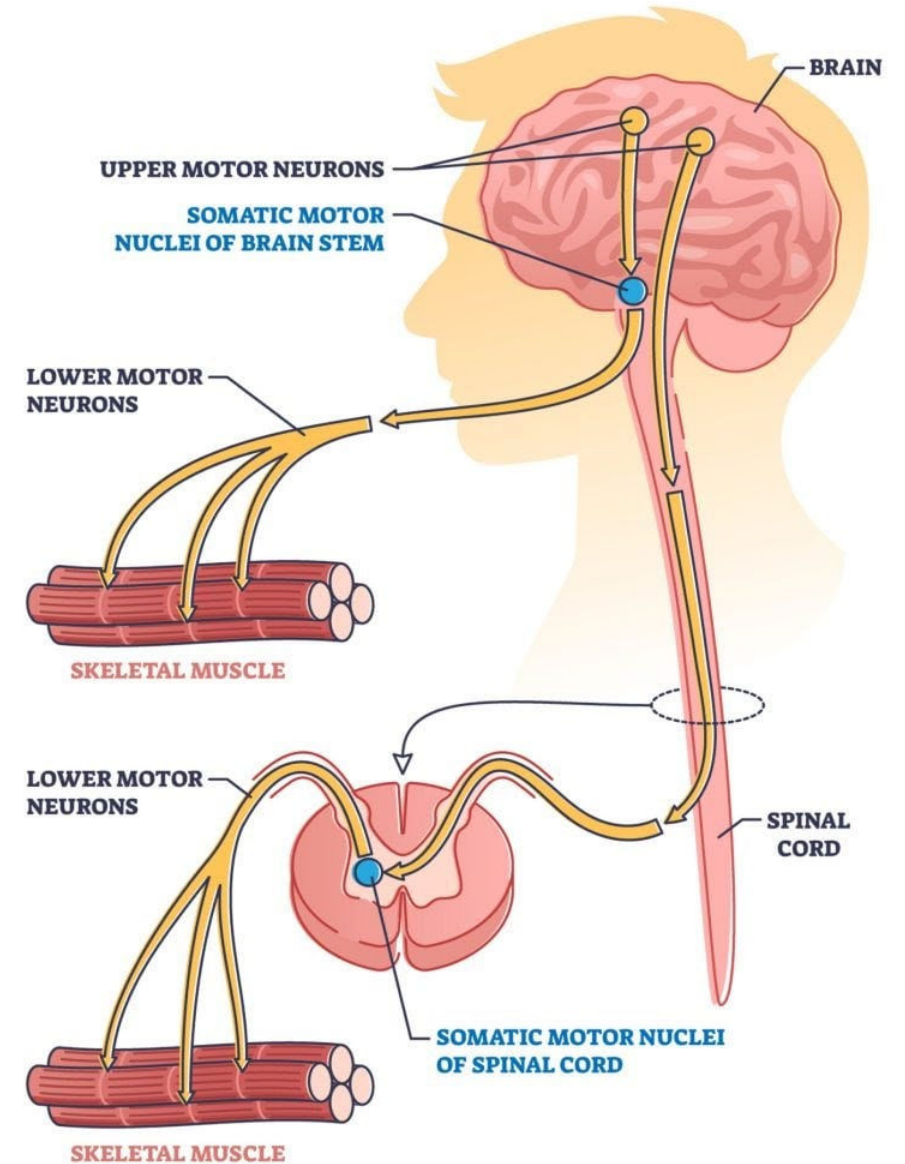
# Outline

- An overview of ALS
- The variable presentations of ALS
  - Age and life stage
  - Level of support
  - Most prominent symptoms
- Decisions one should consider
- Deciding your approach
  - Minimally vs moderately vs maximally aggressive
- The SMA story
- Conclusions



# An Overview of ALS

- A motor neuron disease
- Upper and lower motor neurons break down
- This causes mouth and limb tightness, mouth/limb/diaphragm weakness
- This results in difficulty speaking, swallowing, breathing, moving arms, and moving legs



# An Overview of ALS

Risk factors for ALS include:

- Age – the older one gets, the greater the risk, though ALS can occur at any age
- Men get it more often than women
- Smoking
- Trauma
- US military service
- Genetics
- Clusters



# An Overview of ALS

## Genetics

- 85% of people with ALS do not have a known genetic cause
- 15% of people with ALS have a genetic cause
- This is a rapidly changing field
- Lauren Baldwin will discuss this further later today



# An Overview of ALS

## Disease Progression

- The weakness usually spreads to adjacent body parts
- The disease usually steadily progresses
- The rate of progression is usually consistent
- Big changes can make it seem the disease is progressing in stages – walking, talking, swallowing, etc.
- Everyone is different, but on average, after 5 years, about 20% of people with ALS are still living

# An Overview of ALS

## Diagnosis

- A clinical diagnosis
- Based on what the patient and family report, and what the examination shows
- Progression of motor symptoms by history
- Upper and lower motor neuron findings on examination
- Weakness, atrophy, fasciculations, brisk reflexes, etc.
- Testing for mimics may include bloodwork, MRIs, and EMGs

# Variable Presentation – Age & Life Stage

- Some people develop ALS when they are very young (20s-30s)
- Some develop ALS when they are older (> 75)
- Different life stages include:
  - Job status – near retirement
  - Financial status
  - Marital status
  - Children in the home
  - Caring for others (elderly parents, for example)
  - Major life events in the near future (graduation, weddings, etc.)

# Variable Presentation – Level of Support

- Some people with ALS live alone
- Some live with a significant other, but that person is very ill or debilitated
- Some live with a healthy significant other
- Some live with extended family, who may or may not be able to provide support
- Some live in independent or assisted living
- The type of dwelling can be very important
- Some have family members with medical training, some with technologic/computer expertise

# Variable Presentation – Prominent Symptoms

- Walking problems – foot drop, leg weakness on one or both sides, may require a brace, cane, walker, or wheelchair
- Hand and arm weakness – may affect ability to type, use a smart phone
- Speech – may affect ability to communicate verbally
- Swallowing – may affect ability to eat meals, maintain weight
- Breathing – may limit ability to walk and conduct daily activities

# Decisions to Consider – Quotes

- “We can choose to focus on the beauty of now.” Steve Gleason
- “Intelligence is the ability to adapt to change.” Stephen Hawking
- “I’m not here for a long time, I’m here for a good time.” George Strait
- “Good decisions come from experience. Experience comes from making bad decisions.” Mark Twain

# Decisions to Consider – 2<sup>nd</sup> Opinion

- Get the opinion of a physician that has seen a lot of people with ALS and other neurologic disorders
- There is no limit to the number of opinions one can get, but sometimes 3<sup>rd</sup>, 4<sup>th</sup>, etc. just delay decision making
- There are lot of people and groups that want to make money off this diagnosis, and they will tell people they have Lyme disease, parasites, heavy metal toxicity, etc., and they need special tests only they offer and they need to be on vitamins or antibiotics they sell
- Be weary if someone seems to be financially benefiting from their tests and treatments for ALS or mimics

# Decisions to Consider – Sharing Diagnosis

- I have patients that have kept the diagnosis from everyone – family, work, etc.
- I recommend sharing the diagnosis



# Decisions to Consider – ALS Clinic

- Do I want to attend an ALS clinic?
- Usually every 3 months; some every 6-12 months
- Has been shown to improve outcomes vs going to standard neurologist or PCP
- May be a long distance to travel
- Clinic days can be long
- Can be hard to see others

With ALS



# Decisions to Consider – Mobility Devices

Do I want to get:

- A foot brace
- A cane
- A walker
- A transport wheelchair
- A power wheelchair



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# Decisions to Consider – Breathing Devices

Do I want to get:

- A suction machine
- A cough assist device
- A non-invasive ventilation device
- A tracheostomy and invasive ventilation –  
in the US about 2% of people with ALS choose this



# Decisions to Consider – Feeding Tube

Do I want to:

- Thicken liquids
- Get a feeding tube – about 50% of people with ALS get this
- Think about timing
- Weight loss and low cholesterol are associated with worse outcomes in ALS

# Decisions to Consider – Genetic Testing

Do I want to get:

- Genetic testing
- Consider how it impacts the patient
- Consider how it impacts the family
- It can determine if Qalsody (tofersen) can be used for treatment

# Decisions to Consider – Medications

- Riluzole
- Radicava
- Tofersen
- B12
- Supplements
- Symptomatic treatments –  
Baclofen, Nuedexta, atropine  
drops, etc.
- Consider costs



# Decisions to Consider – Clinical Trials

## Benefits

- Frequent visits
- Access to meds
- Help others

## Downsides:

- Placebo
- Frequent visits
- Lots of travel



**National Library of Medicine**  
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# Decisions to Consider – Hospice

- Hospice and palliative care
- Fantastic nurses, lots of support
- Different care options (home, Hospice house, respite care, etc.)
- Consider what interventions may need to occur before Hospice
- Will be discussed later today by our expert panel



# Your Approach

- No two people are the same (not even twins)
- Think about age, life stage, support, symptoms, disease progression
- Think about your goals
- Discuss with family, friends, and trusted people in your life
- Determine if you want to be minimally, moderately, or maximally aggressive

# Your Approach – Minimally Aggressive

- Attend ALS clinic
- AFOs, canes, walkers, wheelchairs
- Simple communication devices – boogie board, app on phone
- Non-invasive ventilation, cough assist, suction
- B12 and riluzole
- Prioritize time with family, travel, relaxation
- Hospice

# Your Approach – Moderately Aggressive

- Attend ALS clinic
- AFOs, canes, walkers, wheelchairs
- Communication devices
- Non-invasive ventilation, cough assist, suction
- Feeding tube
- B12, riluzole
- Get genetic testing
- Consider clinical trials
- Hospice as disease progresses

# Your Approach – Maximally Aggressive

- Attend ALS clinic
- AFOs, canes, walkers, power wheelchairs
- Non-invasive ventilation and consider tracheostomy
- Eye-gaze communication devices, voice banking
- Feeding tube
- Get genetic testing
- B12, riluzole, Radicava, and supplements
- Enroll in clinical trials; may travel for clinical trials
- May transition to more Hospice care

# Your Approach – Personalize Your Approach

Choose what you want to do

Discuss options with family, friends, trusted advisors

- Attend ALS clinic
- AFOs, canes, walkers, power wheelchairs
- Non-invasive ventilation and consider tracheostomy
- Eye-gaze, voice banking, feeding tube
- Get genetic testing, B12, riluzole, and Radicava
- Enroll in clinical trials; may travel for clinical trials
- Hospice and palliative care

# Hope for the Future – SMA Story

- Like ALS, spinal muscular atrophy (SMA) is a motor neuron disease
- SMA is always genetic (15-20% of ALS is known to be genetic)
- SMA affects kids
- SMA occurs because the SMN1 gene is missing
- There is a back-up SMN2 gene
- Of kids with the most common type of SMA, 92% die before age 2 years old

# Hope for the Future – SMA Story

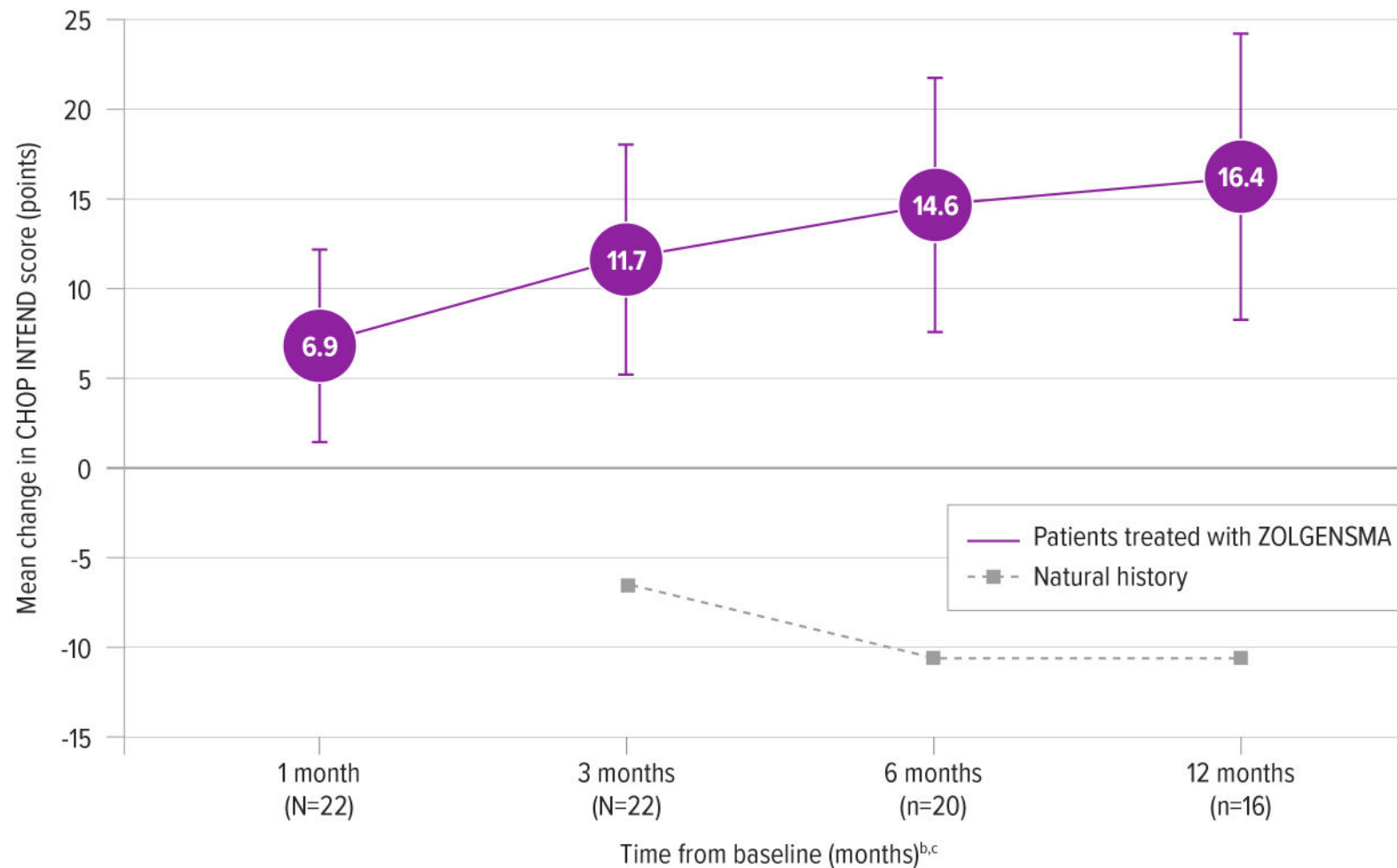
- No powerful treatments were available
- Tracheostomy, ventilators, and feeding tubes were used
- Then Dec 23, 2016 everything changed
- First treatment was approved (Spinraza)
- Second treatment in May 2019 (Zolgensma)
- Third treatment in August 2020 (Evrysdi)
- All genetic therapies, all very expensive, all highly effective

# Hope for the Future – SMA Story

- Now kids are able to roll over, sit up, stand, walk, run, and jump
- Instead of dying before age 2, they may have a normal lifespan
- We now screen for SMA on newborn screen in all 50 states
- In the past 8 years, the disease and how we approach it has completely changed

# Hope for the Future – SMA Story

Mean change in CHOP INTEND from baseline

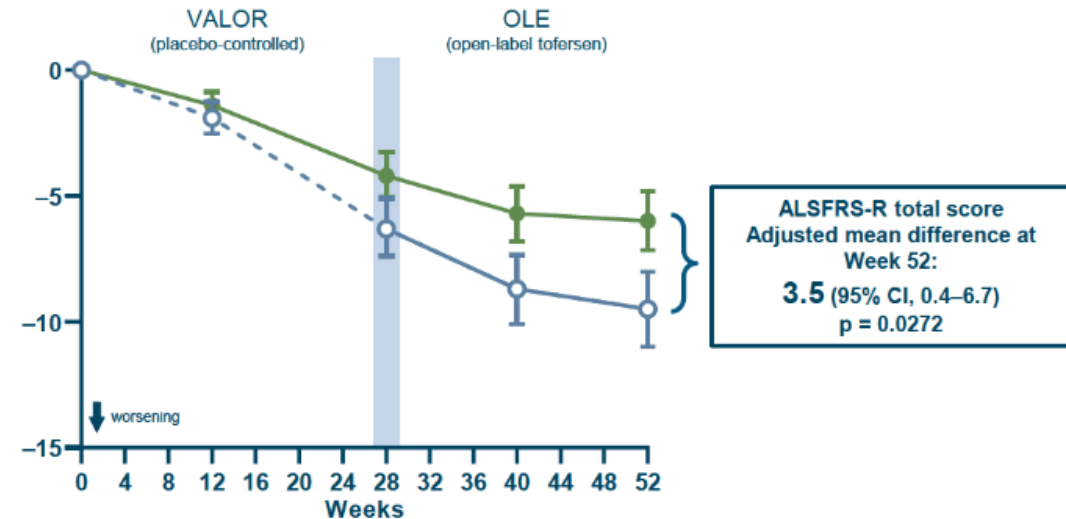


# Hope for the Future – Qalsody

- Qalsody, for ALS with SOD1 genetic changes (about 1% of all people with ALS)

## Effect on Clinical Function

Adjusted mean ( $\pm$ SE) change from baseline in ALSFRS-R total score



○ Placebo → Delayed-start tofersen, n =	36	36	33	29	28
● Early-start tofersen, n =	72	66	63	58	57

ALS = amyotrophic lateral sclerosis; ALSFRS-R = ALS Functional Rating Scale-Revised; OLE = open-label extension  
Analysis is based on ANCOVA model in conjunction with multiple imputation for missing data. The model includes covariates for the corresponding baseline value, baseline plasma NFL, and use of riluzole or edaravone.

# Conclusions

- ALS is different for everyone
- Planning ahead allows someone with ALS to take control of their disease as much as possible and make their own decisions
- Big decisions revolve around clinical trials, feeding tubes, tracheostomies
- Set your goals, involve trusted people in your life
- “Your life is your own. You mold it... All anyone can do is to point out ways and means which have been helpful to others. Perhaps they will serve as suggestions to stimulate your own thinking until you know what it is that will fulfill you.” Eleanor Roosevelt

# Thank You!

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Questions?



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