

HFMSE

Content validity

Clinical meaningfulness

EMA Spinal Muscular Atrophy stakeholder workshop



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DISCLOSURES

SMA

- CONSULTANT for:
 - IONIS Pharmaceuticals
 - BIOGEN
 - ROCHE
 - CYTOKINETICS
- ADVISORY BOARD COMPANIES (Biogen, Roche)
- SPEAKING AGREEMENTS (Biogen)

As clinicians have been very often asked by regulators:

- If what we measure with the outcome measures is clinically relevant

- If acquiring/maintaining an ability on a scale is the same at different ends of disease spectrum or in different age

CAN THE MEASURES WE ARE CURRENTLY USING MEASURE THESE CHANGES?

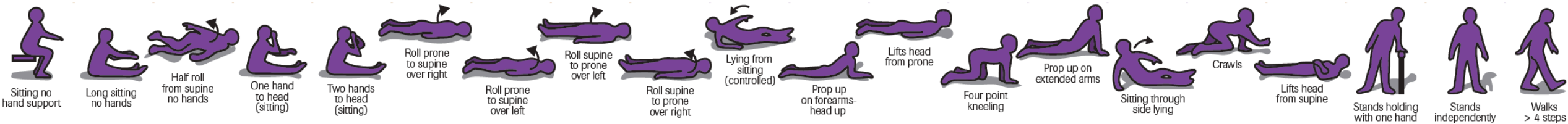
STUDY OBJECTIVES

PHASE 1

EVALUATE CLINICAL RELEVANCE of
HFMSE ITEMS IN REGARDS TO ADLs

PHASE 2

EVALUATE CLINICAL MEANINGFULNESS
of **HFMSE CHANGES**



PHASE 1 - FOCUS GROUPS:

Content validity of HFMSE items

QUALITATIVE STUDY conducted in Italy between June and October 2015 as part of a collaborative project with the two main Italian SMA advocacy groups



63 individuals participated in the focus groups

PARENTS/CAREGIVERS

2-26 Years

17 Mothers & 13 Fathers

5 Ambulant

25 Non ambulant




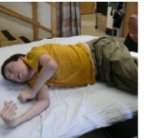
PATIENTS

14-25 Years




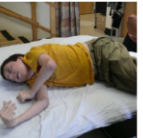
3 Ambulant

22 Non ambulant

Patients and caregivers were given a form describing the items of the HFMSE, with some pictures illustrating the activities included in the scale.





HFMSE ITEM		ACTIVITIES of Daily life
Able to sit on chair or with legs off bed with or without hand support		
Able to bring hands to face at eye level		
Able to bring hands to head		
Roll to side		

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Roll to side		

They were then asked to comment whether each activity assessed in the items could be related to activities of daily living, and if and why this was relevant to them.



HFMSE ITEM		ACTIVITIES of Daily life
SIT ON CHAIR OR WITH LEGS OFF BED WITH OR WITHOUT HAND SUPPORT		<p>-PLAY ON FLOOR WITH FRIENDS</p> <p>-SIT ON:</p> <ul style="list-style-type: none"> • NORMAL SCHOOL CHAIR OR PUBLIC SPACES (STOOLS IN RESTAURANT) • TOILET • CAR <p>INDEPENDENCE OUT OF THE HOUSE</p> <p>DRESS BY HERSELF</p>
ROLL TO SIDE		<p>-SLEEP BY MYSELF IN MY OWN ROOM</p> <p>-CAREGIVER DOES NOT HAVE TO WAKE UP TO TURN PATIENT</p> <p>BE ABLE TO USE SOFA FREELY</p>
BRING HANDS TO HEAD		<p>-WASH, BRUSH, STYLE HAIR</p> <p>-SCRATCH HEAD</p> <p>-DRESS UPPER BODY</p>
ABLE TO HALF KNEEL		<p>-PICK UP OBJECT ON FLOOR</p> <p>-TIE SHOE LACES</p> <p>-PUT AWAY OBJECT ON LOW SURFACE</p> <p>TALK AND BE AT SAME LEVEL OF A CHILD</p>

SELF-CARE

ACCESS AND PARTICIPATION IN SOCIAL ACTIVITIES

INDEPENDENCE

MOBILITY, TRANSFERS

PLAY and EXPERIENCE

Results of the various groups were analyzed by assigning a code to each response and by identifying consistencies across the various groups tabulating the frequency of individual responses in the various subgroups.

HMFSE ITEM	HMFSE activities	Answers	Group			
			Group1	Group 2	Group 3	Group 4 Patients
1	ABLE TO SIT ON CHAIR OR WITH LEGS OFF BED WITH OR WITHOUT HAND SUPPORT	Sitting on normal school chair or public spaces (stools in restaurant)	•	•	•	•
		Sitting on toilet	•	•		•
		Sitting in car			•	
		Independence out of the house	•			•
2	ABLE TO SIT ON FLOOR CROSS LEGGED OR LEGS STRETCHED IN FRONT	Dress by herself/himself		•		
		Play on floor with siblings	•	•	•	•
		Sit on lounge chair, deck-chair		•		•
		Picnic			•	•
		Travel with less equipment	•			
3	ABLE TO BRING HANDS TO FACE AT EYE LEVEL	Inclusion in activities		•		
		Wash face	•	•	•	•
		Brush and style	•	•	•	•
		Eat	•		•	
		Put on eye glasses	•	•		•
		Answer telephone			•	
4	ABLE TO BRING HANDS TO HEAD	Blow nose	•			
		Scratch head	•	•	•	•
		Wash, brush, style hair		•	•	•
		Put on hat	•	•		•
5	ROLL TO SIDE	Dress upper body	•		•	
		Sleep by myself in my own room		•	•	
		Caregiver does not have to wake up to turn him/her	•	•		•
		Help during dressing lying down		•	•	
		Not having to turn head to see	•			
6-7-8-9	ROLL	Play	•	•		
		Sleep well		•	•	
		Sunbathe		•	•	
		Experience space	•			•
		Reach for something at sides when lying down		•		•
10	ABLE TO LYE DOWN FROM SITTING	Independence: lye down and rest when tired	•	•	•	•
		Fun movement when falling	•	•		
		Rest on the back			•	
		Safety: Fall in a controlled way (avoid head trauma)	•			

64% OF ACTIVITIES
66/103
SUGGESTED BY
> ONE GROUP

36% OF ACTIVITIES
37 /103
SUGGESTED BY
ONLY ONE GROUP

ONLY 7
SUGGESTED BY
PATIENTS

PHASE 1 RESULTS

Activities of the HFMSE, known to be relevant in clinical and research practice, are also clinically meaningful to patients and their caregivers

Each activity included in the HFMSE was related to activities of daily living that were relevant to patients and their caregivers, as often suggested by many participants in more than one focus group.

PHASE 2 – Questionnaires/semi-structured interviews

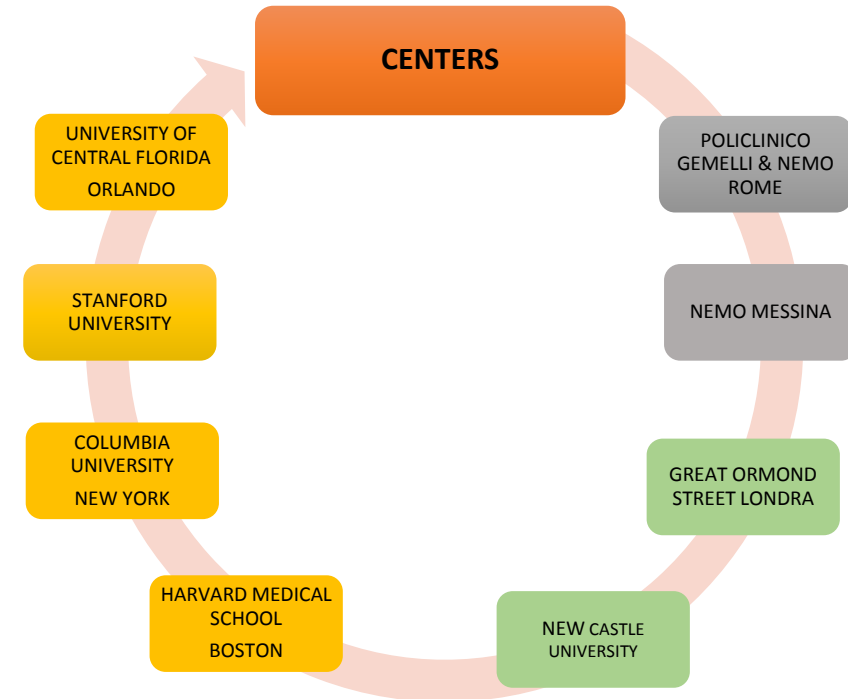
Clinical meaningfulness of HFMSE changes

INTERNATIONAL COLLABORATIVE STUDY
conducted from September 2015 to April 2016

149 caregivers answered

Age of patients: 17 months to 30 years

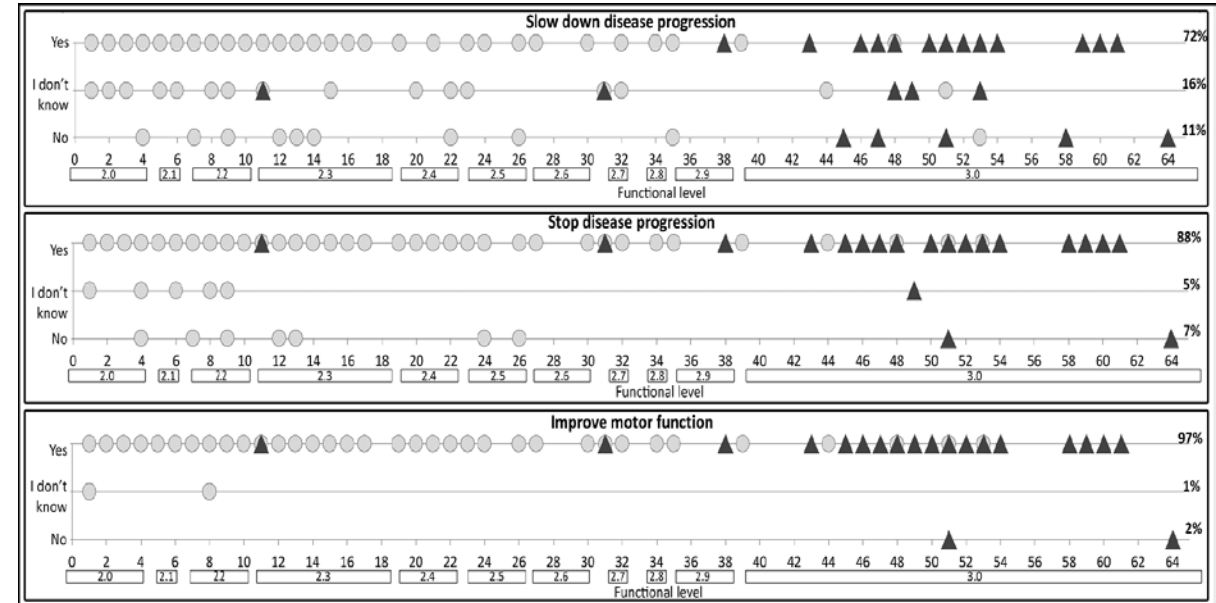
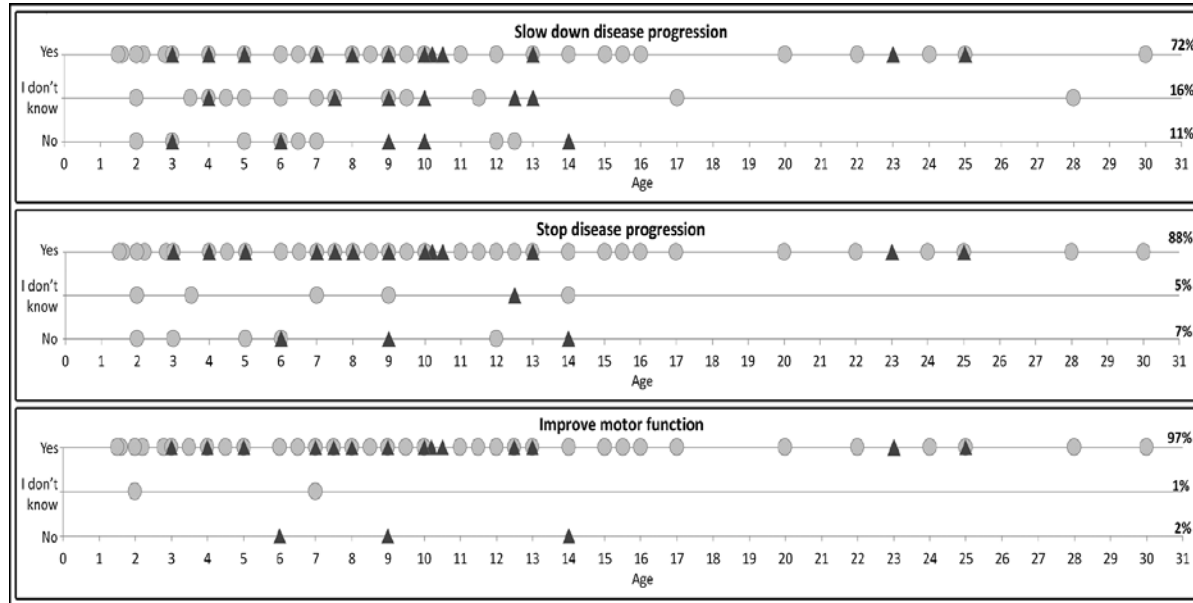
33 ambulant SMA III
7 non-ambulant SMA III
109 non ambulant SMA II



- Open questions covering possible changes that would be meaningful to the patients and their caregivers and their views and expectations regarding a possible participation in a clinical trial.
- When HFMSE functional data of individual patients was available specific questions were tailored to patients' functional level and were used to establish the caregivers view on the clinical relevance of HFMSE changes

“Would you agree to have your child take part in a potential trial if, prospective was to”

- **Slow down a possible decline in motor function for at least two years?**
- **Stop disease progression’**
- **Improve motor function**



72%
SLOW DOWN
DETERIORATION

88%
STOP DETERIORATION

97%
IMPROVE MOTOR
FUNCTION

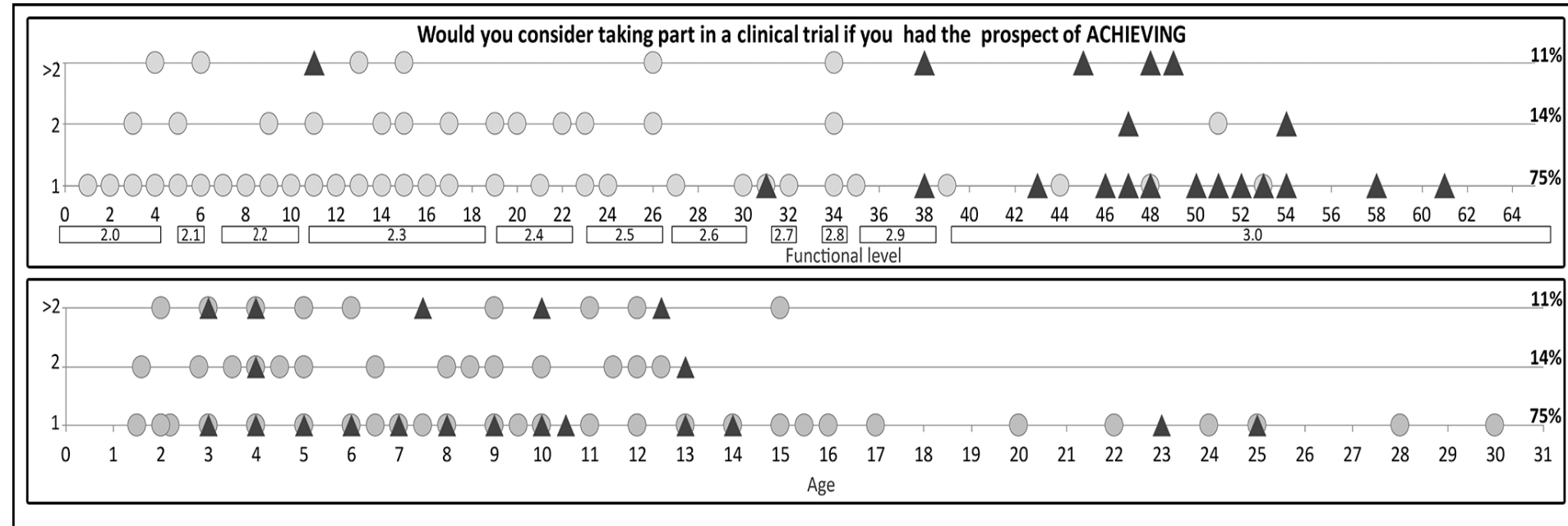
After being informed of the first three items that their child could not achieve on the HFMSE scale:

“Would you consider taking part in a clinical trial if you had the prospective of achieving”

More than 2 abilities

At least 2 of the abilities

At least 1 of the abilities



75% achieve
at least
1 ACTIVITY

89% achieve
at least
2 ACTIVITIES

100% achieve
> 2 ACTIVITIES

STUDY RESULTS

These studies appear to further support the use of the HFMSE as a robust outcome measure in clinical trials

- individual items appear to be all meaningful to patients and carers
- even minimal changes detected on the HFMSE scale, appear to be relevant and would justify participation in a clinical trial.