

# GNE MYOPATHY FUNCTIONAL ACTIVITY SCALE (GNEM-FAS):

## A FOUR YEARS FOLLOW UP IN 10 HIBM PATIENTS

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### INTRODUCTION

- GNE myopathy (GNEM), also known as hereditary inclusion body myopathy (h-IBM), distal myopathy with rimmed vacuoles (DMRV), IBM2 or Nonaka Disease, is a rare, severe and progressive autosomal recessive disorder due to GNE mutations blocking biosynthesis of sialic acid [1]
- The clinical course of h-IBM is characterized by progressive proximal and distal weakness and wasting of both upper and lower limbs with quadriceps sparing, usually beginning after 20 years of age. Diagnosis is based on clinical findings, histopathology (“rimmed vacuoles”) and molecular analysis [2]
- Progressive weakness leads to an increasing disability; patients usually lose ambulation within 10-20 years after onset and they need supportive care for daily activities. A disease-specific measurement of functional activity has been proposed to determine the impact of weakness and mobility restrictions on daily functions to optimize patients care [2]. The goal of this study is to evaluate its application in our cohort of h-IBM patients

### PATIENTS AND METHODS

- We present a cohort of 11 patients (8 F and 3 M) with h-IBM. Age at onset ranged between 19 and 32 years (medium value: 24 years). All patients have been genetically defined for GNE variants. Two of them (1 and 2) are enrolled in UX001-CL301 trial with Aceneuramic Acid
- After clinical evaluation, GNE myopathy functional activity scale (GNEM-FAS) was administered at the first visit (T0) performed on 2013 (when GNEM-FAS was validated) and at the last visit (T1) after a 4 years follow-up
- GNEM-FAS (Table 1) consists of a 25-item questionnaire. Each item was rated from 0 to 4 with higher scores representing better function. Total scores range from 0 to 100; subscale scores range from 0 to 40 for **Mobility**, 0–32 for **upper extremity** use (UE) and 0–28 for **Self-Care** [3].

Mobility	Activity Level				
	INDEPENDENT NO limitations NO compensations NO devices	INDEPENDENT Slowly/Some difficulty May use orthotics NO external support	WITH devices and/or external support	DEPENDENT Requires MIN- MOD assist of person	DEPENDENT Unable or requires MAX assist of person
1. Turn in Bed	4	3	2	1	0
2. Supine to Sit	4	3	2	1	0
3. Sit to Stand	4	3	2	1	0
4. Walking	4	3	2	1	0
5. Stepping up on Curb	4	3	2	1	0
6. Climbing Stairs	4	3	2	1	0
7. Reach to Floor and Recover (e.g. pick up object from floor)	4	3	2	1	0
8. Floor to Standing	4	3	2	1	0

  

Additional Mobility Items	Activity Level				
	INDEPENDENT Runs fast NO limitations NO compensations NO devices	INDEPENDENT Runs fast NO limitations NO compensations NO devices	WITH devices and/or external support	DEPENDENT Requires MIN- MOD assist of person	DEPENDENT Unable or requires MAX assist of person
9. Running	4	3	2	1	0
10. Vertical Jump (able to clear both feet)	4	3	2	1	0

Table 1: GNEM-FAS

Upper Extremity	Activity Level				
	INDEPENDENT NO limitations NO compensations NO devices	INDEPENDENT Slowly/Some difficulty NO modifications NO external support	WITH devices modifications and/ or external support	DEPENDENT Requires MIN- MOD assist of person	DEPENDENT Unable or requires MAX assist of person
11. Making Fist (all fingers flexing fully)	4	3	2	1	0
12. Writing with pencil or pen	4	3	2	1	0
13. Hand to mouth (e.g. lifting filled glass or mug)	4	3	2	1	0
14. Cutting foods with utensils (e.g. meat with regular knife)	4	3	2	1	0
15. Carrying objects (e.g. bag of med weight groceries)	4	3	2	1	0
16. Opening doors	4	3	2	1	0
17. Opening drink bottles (e.g. small mouth water bottle)	4	3	2	1	0
18. Lifting objects overhead (e.g. med weight object on high shelf)	4	3	2	1	0

Self-Care	Activity Level				
	INDEPENDENT NO limitations NO compensations NO devices	INDEPENDENT Slowly/Some difficulty NO devices NO external support	WITH devices modifications and/ or external support	DEPENDENT Requires MIN- MOD assist of person	DEPENDENT Unable or requires MAX assist of person
19. Brushing teeth	4	3	2	1	0
20. Brushing/washing hair	4	3	2	1	0
21. Dressing upper body (e.g. shirt overhead)	4	3	2	1	0
22. Dressing lower body (e.g. pants in standing)	4	3	2	1	0
23. Buttoning	4	3	2	1	0
24. Bathing (consider tub and shower)	4	3	2	1	0
25. Toileting	4	3	2	1	0
(items 1-25) COLUMN TOTALS					

### RESULTS

PATIENTS	GENDER	AGE	AGE AT ONSET	GNEM-FAS T0			GNEM-FAS T0	GNEM-FAS T1			GNEM-FAS T1	LOSS OF AMBULATION (YEARS AFTER ONSET)
				MOBILITY	UE	SELF CARE		MOBILITY	UE	SELF CARE		
1	F	45	30	24	30	27	82	23	27	27	77	WALKING
2	F	30	27	16	32	27	85	16	29	27	76	WALKING
3	F	28	19	26	30	26	79	2	12	15	29	6
4	F	28	19	26	29	25	79	3	11	14	28	6
5	F	39	22	9	25	21	55	1	16	11	28	13
6	F	49	23	5	26	15	46	1	18	10	29	20
7	F	56	28	8	30	22	56	2	19	10	31	20
8	M	31	19	24	30	27	81	2	19	15	36	10
9	M	31	26	14	29	23	59	2	23	14	39	3
10	F	39	22	21	31	21	57	2	19	12	33	6
11	M	60	32	10	25	17	52	1	13	7	21	22
Medium value		39.6	24.2	16.9	28.8	22.8	66.4	5	18.7	14.7	38.8	11.7

Table 2: Patient's data

- The mean GNEM-FAS total score was **66.4** out of 100 (46-85) at the first visit (T0) and **38.8** out of 100 (28-77) at the last visit (T1)
- At T0, mobility subscores averaged **42%**, Upper Extremities (UE) **92%**, and Self-Care **64%** of the maximum possible
- At T1, mobility averaged **12%**, UE **58%** and Self-Care **52%** of the maximum level
- The most involved domain was the mobility; in fact, 80% of our patients lost ambulation
- 7 out of 11 pts needed wheelchair within 11 years since the onset of first symptoms

### DISCUSSION

- The GNEM-FAS is a novel, disease-specific scale that could be successfully administered to ambulatory adult patients as a measure of their physical functions
- Mobility, upper extremities use and self-care need to be carefully assessed to determine the impact of weakness and mobility restrictions on daily functions
- GNEM-FAS is a helpful tool to assess the progression of the disease; it is appropriately combined with myometry use and quality of life (InQoL) assessment in current trials

### Bibliography

1. Das B, Goyal MK, Bhatkar SR, Vinny PW, Modi M, Lal V, Gayathri N, Mahadevan A, Radotra BD. Hereditary inclusion body myopathy: A myopathy with unique topography of weakness, yet frequently misdiagnosed: Case series and review of literature. Ann Indian Acad Neurol. 2016 Jan-Mar;19(1):119-22.
2. Argov Z, Caraco Y, Lau H, Pestronk A, Shieh PB, Skrinar A, Koutsoukos T, Ahmed R, Martinisi J, Kakkis E. Aceneuramic Acid Extended Release Administration Maintains Upper Limb Muscle Strength in a 48-week Study of Subjects with GNE Myopathy: Results from a Phase 2, Randomized, Controlled Study. J Neuromuscul Dis. 2016 Mar 3;3(1):49-66.
3. A.M. Skrinar, Z. Argov, Y. Caraco, E. Kolodny, H. Lau, A. Pestronk, P. Shieh, F. Bronstein, A. Esposito, Y. Feinsod-Meir, J. Florence, E. Fowler, M. Greenberg, E. Malkus, O. Rebibo, C. Siener. GNE myopathy functional activity scale (GNEM-FAS): Development of a disease-specific instrument for measuring function and independence. Neuromuscular Disorders Volume 23, Issues 9–10, October 2013, Page 755.