Supplemental material

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J Neurol Neurosurg Psychiatry

Supplementary Table 1

Clinical characteristics of the 40 patients with SMA type I before nusinersen treatment

	South Korea	Taiwan	Hong Kong SAR	Total n (%)
No. of patients who received EAP	18	15	7	40
No. of patients identified by newborn screening	0	9	0	9 (22.5%)
Age of symptom onset: median age in months (range)	3.00 (0.03 -6)	3.37 (0.03 - 5)	3.0 (1-4.5)	3.0 (0.03-6)
Nusinersen initiation age: median age in months (range)	23.0 (2-79)	4.9 (0.35-191)	51 (19 -294)	20.0 (0.35 - 294)
SMN1 mutation				
Homozygous exon 7 deletion	18	14	6	38 (95%)
Compound heterozygous exon 7 deletion & point mutation	-	1	1	2 (5%)
SMN2 copies				
1 copy	1	-	-	1 (2.5%)
2 copies	13	9	3	25 (62.5%)
3 copies	4	6	4	14 (35.0%)
Gestational age				
Prematurity (<37 weeks gestation)	2	1	0	3 (7.5%)
Full term (≥37 weeks gestation)	16	14	7	37 (92.5%)
Nutritional status				
Body weight <3rd percentile	10	1	0	11 (27.5%)
Body weight ≥3rd percentile	8	14	7	29 (72.5%)
Ventilation status				
No ventilator support	3	5	1	9 (22.5%)
Need ventilator support	15	10	6	31 (77 .5%)
NIV <16 h per day	3	9	3	15
NIV >16 h per day	3	0	3	6
IV	9	1	0	10
Feeding status				
Oral	5	8	1	14 (35.0%)
Tube feeding	13	7	6	26 (65.0%)
Feeding tube	5	1	1	7
Gastrostomy	8	6	5	19
Musculoskeletal status				
Scoliosis/kyphoscoliosis	5	2	4	11 (27.5%)
Spinal fusion	0	0	1	1
	7	2	5	14 (35.0%)
Hip subluxation/dislocation				
Hip dislocation (both)	3	1	3	7
Hip subluxation (both/unilateral)	4 (2/2)	1 (1/0)	2 (2/0)	7 (5/2)

Abbreviation: EAP – Expanded Access Program; NIV – non-invasive ventilation; IV – invasive ventilation

Supplementary Table 2

Number of patients receiving Nusinersen treatment and CHOP INTEND and HINE-2 Evaluation

	South Korea	Taiwan	Hong Kong SAR	Total
Participating Hospitals	5	2	1	8
Number of patients receiving EAP	18	15	7	**40**
Age of nusinersen initiation: median age in months (range)	23.0 (2-79)	4.9 (0.35-191)	51 (19 -294)	20.0 (0.35 - 294)
Number of deaths during 1st year treatment	1	0	0	1
Number of patients dropped out during treatment	1	0	0	1
Number of patients with sedation	LA only (14) IV only (1) LA + Oral + IV (3)	LA only (2) IV only (9) LA+IV (4)	LA only (2) IV only (5)	LA only (18) IV only (15) Combined (7)
Number of patients who required X-ray guidance or special arrangements for intrathecal drug delivery	Fluoroscopic guidance (8)	(0)	Fluoroscopic guidance (1) 3D dynamic CT guidance (1) Port-A-Cath implantation (1)	Fluoroscopic guidance (9) 3D dynamic CT guidance (1) Port-A-Cath implantation (1)
Number of patients undergone motor assessment				
CHOP INTEND Evaluation				
M0	12	3	6	21
M6	12	3	6	21
M10	9	3	6	18
HINE-2 Evaluation				
M0	18	13	6	37
M6	15	13	6	34
M10	12	12	6	30

Abbreviation: LA = local anaesthetics; IV = intravenous sedation; LP = lumbar puncture; CT = computed tomography

Supplementary Table 3

CHOP INTEND evolution of patients according to *SMN2* copy number and age of nusinersen initiation

Characteristics	Total (n=40)[a]	1 copy of *SMN2* (n=1)[a]	2 copies of *SMN2* (n=25)[a]	3 copies of *SMN2* (n=14)[a]
Sex, M: F, n	18:22	1:0	10:15	7:7
Age at first symptoms[a]	3.0 (0.0-6.0)	0.0	2.0 (0.0-6.0)	4.5 (1.0-6.0)
Age at first injection[a]	20.0 (0.35-294.0)	2.0	19.0 (0.35-140.0)	25.3 (4.0-294.0)
CHOP INTEND score				
M0[a]	12.0 (0.0-60.0), n=23	12.0, n=1	4.0 (0.0-39.0), n=13	27.0 (0.0-60.0), n=9
M6[a]	30.0 (1.0-64.0), n=21	39.0, n=1	8.0 (1.0-52.0), n=12	34.0 (21.0-64.0), n=8
M10[a]	31.5 (1.0-64.0), n=20	42.0, n=1	10.0 (1.0-62.0), n=11	34.0 (24.0-64.0), n=8
Time-effect p value[b]	<0.001	/	0.006	<0.001
Delta M6-M0[c]	7.0 (0.0-39.0), p<0.001	27.0	3.0 (0.0-39.0), p=0.019[d]	8.5 (1.0-19.0), p=0.005[d]
Delta M10-M0[c]	8.5 (0.0-49.0), p<0.001	30.0	3.0 (0.0-49.0), p=0.030[d]	8.5 (4.0-19.0), p=0.003[d]
CHOP INTEND score (Age ≤2 years old at onset of treatment)				
M0[a]	11.0 (0.0-60.0), n=12			
M6[a]	34.0 (2.0-64.0), n=11			
M10[a]	38.0 (3.0-64.0), n=10			
Time-effect p value[b]	0.002			
Delta M6-M0c	5.0 (1.0-39.0), p=0.014			
Delta M10-M0[c]	11.0 (1.0-49.0), p=0.014			
CHOP INTEND score (Age >2 years old at onset of treatment)				
M0[a]	13.0 (0.0-31.0), n=11			
M6[a]	23.0 (1.0-46.0), n=10			
M10[a]	24.5 (1.0-47.0), n=10			
Time-effect p value[b]	<0.001			
Delta M6-M0[c]	6.5 (0.0-19.0), p=0.006			
Delta M10-M0[c]	6.5 (0.0-19.0), p=0.005			

Abbreviations: CHOP INTEND = Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders; M0 = before treatment; M6 = 6 months of treatment; M10 = 10 months of treatment; *SMN* = survival motor neuron.

[a] Data are listed as median (range) in months.

[b] One-way-repeated-measures ANOVA.

[c] Paired T-test.

[d] The multiple regression demonstrated that there was significant difference in the changes of the CHOP INTEND scores Delta M6-M0 and Delta M10-M0, between the two groups with 2 and 3 *SMN2* copies with a standardized coefficients β of 0.440 (p<0.001).

CHOP-INTEND scores were missing in 19 patients, due to the following two reasons: 1). 12 patients did not have CHOP-INTEND performed: 2). 7 patients had incomplete CHOP-INTEND scores at either baseline or at M6 or M10 so no paired data were available for analysis.

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Supplementary Table 4

Multiple linear regression model for changes in HINE-2 (M10-M0) and CHOP INTEND (M10-M0) scores

Dependent variables	Factors	Correlation	P-value	Standardized Coefficients Beta	P-value
Changes in HINE-2 scores N=32 $r^2=0.479$	Disease duration	-0.391	0.027*	-0.302	0.069
	SMN2 copy number	0.144	0.430	0.099	0.607
	Baseline HINE-2 scores	0.377	0.033*	0.292	0.117
	Newborn screening	0.557	0.001*	0.424	0.009*
Changes in CHOP-INTEND Scores N=18 $r^2=0.159$	Disease duration	-0.172	0.494	0.046	0.889
	SMN2 copy number	-0.292	0.240	-0.506	0.195
	Baseline CHOP-INTEND scores	0.047	0.852	0.486	0.338
	Newborn screening	0.018	0.942	-0.219	0.623

* $p < 0.05$

The multiple linear regression shown that only newborn screening was independently associated with delta HINE-2 scores with the model r-square value of 0.479, adjusted beta=0.424 (p=0.009).

We could not find any predictor variable for the Delta CHOP INTEND (M10-M0) scores. We understand the limitations when interpreted the findings as only half of this cohort had paired CHOP INTEND scores at M0 and M10 (n=18), and only one patient with paired CHOP INTEND scores was identified by newborn screening.

Supplementary Table 5

Changes in the requirement of ventilation support at M6 and M10, compared to baseline M10

	Ventilator support					Patient number (n)
						Change in ventilation status
	No Need	Nocturnal NIV	Nocturnal & Day < 24h NIV	24 h NIV	24 h IV	
For all 40 patients receiving nusinersen treatment						
M0						
Patient number	11	12	3	10	4	**n = 40**
1st Tx age (months)	(0.35 -24)	(1.3-191)	(53.6-294)	(2-150)	(5 -140)	
M10 - M0						
Patient number	11	12	3	8 #, @	4	**n = 38 #, @**
Status same	8	9	2	2	1	Same Ventilation setting: 57.8% (22/38 patients)
↓ ventilation need	-	1 off NIV 2 ↓ setting	1 to Noct. NIV -	3 ↓ setting	1 to Noct. IV	↓ ventilation need: 21.1% (8/38 patients)
↑ ventilation need	3 started NIV	-		3 ↑ setting	2 ↑ setting	↑ ventilation need: 21.1% (8/38patients)

Findings: Among the 38 patients who continued the EAP at M10, 57.8% of patients had same ventilation status. An equal percentage (21.1%) of patients had a decreased ventilation need (off NIV, ↓ NIV duration, ↓ ventilation setting) as those with an increased ventilation need (need to start on nocturnal NIV, ↑ ventilation setting).

Abbreviations: M0 = before treatment; M6 = 6 months of treatment; M10 = 10 months of treatment; h=hours; Noct. = nocturnal; NIV = Non-invasive ventilation; IV= Invasive ventilation; m=months; Ax = assessment; Tx age = Nusinersen treatment starting age; # 1 patient died before M6 treatment; @ 1 patient dropped out after M6 treatment

Figure Legends

Supplementary Figure 1. Longitudinal HINE-2 score according to the age of first nusinersen treatment. Different shapes of dots indicate different months of nusinersen treatment (M0: circle; M6: triangle; M10: square). Total number of patients = 35. *SMN2* copy numbers and newborn screening are color-coded.

Supplementary Figure 2. Longitudinal CHOP INTEND score according to the age of first nusinersen treatment. Different shapes of dots indicate different months of nusinersen treatment (M0: circle; M6: triangle; M10: square). Total number of patients = 25. Five patients had <3 evaluations. *SMN2* copy numbers and newborn screening are color-coded.