

The Safety and Effectiveness of Chenodeoxycholic Acid Treatment in Patients with Cerebrotendinous Xanthomatosis: Two Retrospective Cohort Studies

Neurological Sciences

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SUPPLEMENTAL MATERIAL

Statistical Analyses (Both Studies)

Descriptive statistics are presented, including patient number (n) and frequency (%), arithmetic mean, 95% confidence intervals (95% CI), and median. Missing values were included in the denominator count when computing percentages. Changes from baseline at V1, V2 and CCC visit were evaluated using a paired t-test, and statistical significance declared if the rounded p-value was ≤ 0.05 . In the NL study, sub-analyses were conducted based on patients' age at treatment initiation (<21 or ≥ 21 years), as studies have demonstrated differences in outcomes depending on age at diagnosis and at treatment initiation [1].

The analysis of 7 α -hydroxy-4-cholesten-3-one was based on a mixed model for repeated measures, with change from baseline in 7 α -hydroxy-4-cholesten-3-one at V1 and V2 as dependent variables, visit as a fixed effect, and the baseline and baseline \times visit interaction as covariates. An unstructured covariance matrix was considered, and the Kenward-Roger adjustment was used for the degrees of freedom.

Supplemental Table 1. Urinary bile alcohols (NL study only; evaluable population)

PT Visits	Baseline Visit				
n (%)	Elevated	Mildly elevated	Normal	Missing/not done	Total
V1 (n=31)					
Elevated	3 (9.7)	0 (0.0)	0 (0.0)	0 (0.0)	3 (9.7)
Mildly elevated	12 (38.7)	0 (0.0)	0 (0.0)	0 (0.0)	12 (38.7)
Normal	6 (19.4)	0 (0.0)	0 (0.0)	0 (0.0)	6 (19.4)
Missing/not done	8 (25.8)	0 (0.0)	0 (0.0)	2 (6.5)	10 (32.3)
Total	29 (93.5)	0 (0.0)	0 (0.0)	2 (6.5)	31 (100.0)
p-value (Test of symmetry) <0.001					
V2 (n=31)					
Elevated	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Mildly elevated	7 (22.6)	0 (0.0)	0 (0.0)	0 (0.0)	7 (22.6)
Normal	10 (32.3)	0 (0.0)	0 (0.0)	2 (6.5)	12 (38.7)
Missing/not done	12 (38.7)	0 (0.0)	0 (0.0)	0 (0.0)	12 (38.7)
Total	29 (93.5)	0 (0.0)	0 (0.0)	2 (6.5)	31 (100.0)
p-value (Test of symmetry) <0.001					
CCC visit (n=31)					
Elevated	3 (9.7)	0 (0.0)	0 (0.0)	0 (0.0)	3 (9.7)
Mildly elevated	4 (12.9)	0 (0.0)	0 (0.0)	0 (0.0)	4 (12.9)
Normal	6 (19.4)	0 (0.0)	0 (0.0)	1 (3.2)	7 (22.6)
Missing/not done	16 (51.6)	0 (0.0)	0 (0.0)	1 (3.2)	17 (54.8)
Total	29 (93.5)	0 (0.0)	0 (0.0)	2 (6.5)	31 (100.0)
p-value (Test of symmetry) <0.001					

Abbreviations: CCC: Current clinical condition; NL: The Netherlands; V1: Post-treatment visit 1; V2: Post-treatment visit 2.

Supplemental Table 2. Adverse events and serious adverse events (safety populations)

	NL Study (N=35)		IT Study (N=28)	
	n (%)	Number of events	n (%)	Number of events
Any AE	26 (74.3)	76	9 (32.1)	16
Surgical and medical procedures	11 (31.4)	18	6 (21.4)	9
Musculoskeletal and connective tissue disorders	6 (17.1)	7	-	-
Gastrointestinal disorders	5 (14.3)	7	2 (7.1)	2
General disorders and administration site conditions	5 (14.3)	5	-	-
Injury, poisoning and procedural complications	5 (14.3)	5	1 (3.6)	1
Cardiac disorders	4 (11.4)	5	-	-
Skin and subcutaneous tissue disorders	4 (11.4)	4	-	-
Hepatobiliary disorders	3 (8.6)	3	1 (3.6)	1
Infections and infestations	3 (8.6)	4	-	-
Metabolism and nutrition disorders	3 (8.6)	3	-	-
Nervous system disorders	3 (8.6)	3	-	-
Eye disorders	2 (5.7)	2	1 (3.6)	1
Immune system disorders	2 (5.7)	2	-	-
Psychiatric disorders	2 (5.7)	2	-	-
Respiratory, thoracic and mediastinal disorders	2 (5.7)	2	-	-
Vascular disorders	2 (5.7)	2	-	-
Investigations^[a]	1 (2.9)	1	-	-
Renal and urinary disorders	1 (2.9)	1	-	-
Neoplasms benign, malignant and unspecified (including cysts and polyps)	-	-	1 (3.6)	1
Pregnancy, puerperium and perinatal conditions	-	-	1 (3.6)	1
Any Serious AE	7 (20.0)	9	9 (32.1)	15
Surgical and medical procedures	3 (8.6)	3	6 (21.4)	9

Gastrointestinal disorders	-	-	2 (7.1)	2
Cardiac disorders	1 (2.9)	1	-	-
Eye disorders	-	-	1 (3.6)	1
Injury, poisoning and procedural complications	1 (2.9)	1	1 (3.6)	1
Musculoskeletal and connective tissue disorders	1 (2.9)	1	-	-
Psychiatric disorders	1 (2.9)	1	-	-
Renal and urinary disorders	1 (2.9)	1	-	-
Respiratory, thoracic and mediastinal disorders	1 (2.9)	1	-	-
Neoplasms benign, malignant and unspecified (including cysts and polyps)	-	-	1 (3.6)	1
Pregnancy, puerperium and perinatal conditions	-	-	1 (3.6)	1

[a] Weight increased. Patients are only counted once for each row in the column "n (%)" and percentages are calculated based on the number of patients (N). Abbreviations: IT: Italy; NL: The Netherlands.

REFERENCE

1. Yahalom G, Tsabari R, Molshatzki N, Ephraty L, Cohen H, Hassin-Baer S (2013) Neurological outcome in cerebrotendinous xanthomatosis treated with chenodeoxycholic acid: early versus late diagnosis. *Clinical neuropharmacology* 36 (3):78-83. doi:10.1097/WNF.0b013e318288076a