Dossier zur Nutzenbewertung gemäß § 35a SGB V

Pegzilarginase (Loargys®)

Immedica Pharma Germany GmbH

Modul 4A Anhang 4-G

Arginase-1-Mangel, auch bekannt als Hyperargininämie, bei Erwachsenen, Jugendlichen und Kindern ab 2 Jahren

Ergänzende Informationen zur Studie PEACE

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Abkürzungsverzeichnis

Abkürzung	Bedeutung
2MWT	2-Minuten-Gehtest (*2-Minute Walking Test*)
9HPT	9-Hole Pegboard Test
ADA	Anti-Arzneimittel Antikörper (*Anti-Drug Antibodies*)
AESI	Unerwünschte Ereignisse von besonderem Interesse (*Adverse Event of Special Interest*)
CaGI-C	*Caregiver Global Impressions of Change*
CaGI-S	*Caregiver Global Impressions of Severity*
CGI-C	*Clinician Global Impressions of Change*
CGI-S	*Clinician Global Impressions of Severity*
FMS	*Functional Mobility Scale*
GAA	Guanidinoessigsäure (*Guanidinoacetic Acid*)
GC	Guanidinoverbindung (*Guanidino Compund*)
GFAQ	*Gillette Functional Assessment Questionnaire*
GMFCS	*Gross Motor Function Classification System*
GMFM	*Gross Motor Function Measure-88*
GVA	Alpha-Keto-Delta-Guanidino-Valeriansäure (*Alpha-Keto-Delta-Guanidinovaleric Acid*)
CI	Konfidenzintervall (*Confidence Interval*)
LSM	Mittleren Veränderungen auf Basis der Kleinste-Quadrate-Methode (*Least Squares Mean*)
LSMD	Differenz der mittleren Veränderungen auf Basis der Kleinste-Quadrate-Methode (*Least Squares Mean Difference*)
MMRM	Gemischtes Modell für wiederholte Messungen (*Mixed Model for Repeated Measurements*)
NAA	N-α-Acetylarginin
NRI	*Non-Responder-Imputation*
OR	*Odds Ratio*
PedsQL	*PedsQL: Pediatric Quality of Life Inventory,*
PT	*Preferred Terms* nach MedDRA
RD	Risk Difference
RR	Risk Ratio
SAS	Statistical Analysis System

Abkürzung	**Bedeutung**
SD	Standardabweichung (*Standard Deviation*)
SE	Standardfehler (*Standard Error*)
SMD	Standardisierte Mittelwertdifferenzen
SOC	*System Organ Class* nach MedDRA
TEAE	Behandlungsbedingte unerwünschte Ereignisse (*Treatment Emergent Adverse Event*)
VABS-II	*Vineland Adaptive Behavior Scale, Second Edition*
WAIS-IV	*Wechsler Adult Intelligence Scale, Fourth Edition*
WHO	*World Health Organization*
WIS	*Wechsler Intelligence Scales*
WISC-V	*Wechsler Intelligence Scale for Children, Fifth Edition*
WPPSI-IV	*Wechsler Preschool and Primary Scale of Intelligence, Fourth Edition*

4 Ergänzende Informationen zur Studie PEACE

4.1 Hintergrund

Auf den nachfolgenden Seiten finden sich alle im Dossier angeführten ergänzenden Analysen, im statistischen Analyseplan präspezifizierte Sensitivitätsanalysen, alle Subgruppenanalysen für die Hauptanalysen aller patienten-relevanten Endpunkte sowie eine Auflistung der Begleitmedikation, die während der Studie von ≥ 2 Patienten eingenommen wurde. Für die Verträglichkeit auf Ebene der SOC/PT wurden darüber hinaus Subgruppenanalysen für jegliche und schwere UE sowie SUE durchgeführt.

Mit Ausnahme der Abschnitte 4.2, 4.3 und 4.8 werden alle Analysen als Ausgabe der Statistik-Software dargestellt

4.2 Begleitmedikation

PEACE	**Pegzilarginase[a] (N = 21)**	**Placebo[a] (N = 11)**	**Gesamt (N = 32)**
ATC-Klasse, n (%) Bevorzugter Name, n (%)			
Jegliche Begleitmedikation	21 (100)	11 (100)	32 (100)
Amide	2 (9,5)	5 (45,5)	7 (21,9)
Lidocain	2 (9,5)	4 (36,4)	6 (18,8)
Aminosäuren und Derivate	3 (14,3)	1 (9,1)	4 (12,5)
Aminosäuren und Derivate	2 (9,5)	0	2 (6,3)
Aminosäuren/Kohlenhydrate/Mineralstoffe/ Vitamine, Kombinationen	14 (66,7)	7 (63,6)	21 (65,6)
Nicht näher spezifizierte Aminosäuren/Kohlenhydrate/Mineralstoffe/ Fette/ Vitamine	3 (14,3)	2 (18,2)	5 (15,6)
Aminosäuren/Kohlenhydrate/Mineralstoffe/Vitamine, Kombinationen	2 (9,5)	1 (9,1)	3 (9,4)
Cyclinex 2	4 (19,0)	2 (18,2)	6 (18,8)
Dialamine	2 (9,5)	2 (18,2)	4 (12,5)
Essenzielle Aminosäuren	6 (28,6)	2 (18,2)	8 (25,0)

PEACE	**Pegzilarginase[a] (N = 21)**	**Placebo[a] (N = 11)**	**Gesamt (N = 32)**
ATC-Klasse, n (%) Bevorzugter Name, n (%)			
Aminoalkylether	4 (19,0)	1 (9,1)	5 (15,6)
Diphenhydramin	2 (9,5)	1 (9,1)	3 (9,4)
Anilide	10 (47,6)	3 (27,3)	13 (40,6)
Acetaminophen	2 (9,5)	1 (9,1)	3 (9,4)
Paracetamol	6 (28,6)	2 (18,2)	8 (25,0)
Elektrolytlösungen	1 (4,8)	2 (18,2)	3 (9,4)
Natriumchlorid	0	2 (18,2)	2 (6,3)
Fette/Kohlenhydrate/Proteine/Mineralstoffe/Vitamine, Kombinationen	1 (4,8)	2 (18,2)	3 (9,4)
Nicht näher spezifizierte Aminosäuren/Kohlenhydrate/Mineralstoffe/ Proteine/ Fette/ Vitamine	1 (4,8)	2 (18,2)	3 (9,4)
Allgemeine Diätetika	7 (33,3)	1 (9,1)	8 (25,0)
Allgemeine Diätetika	3 (14,3)	0	3 (9,4)
Nicht näher bestimmte Diätetika	3 (14,3)	1 (9,1)	4 (12,5)
Histamin-H_2-Rezeptorantagonisten	2 (9,5)	3 (27,3)	5 (15,6)
Famotidin	0	3 (27,3)	3 (9,4)
Pepcid (Famotidin)	2 (9,5)	0	2 (6,3)
Influenza-Impfstoffe	5 (23,8)	2 (18,2)	7 (21,9)
Grippe	3 (14,3)	0	3 (9,4)
Multivitamine mit Mineralstoffen	6 (28,6)	3 (27,3)	9 (28,1)
Nicht näher spezifizierte Mineralstoffe/ Vitamine	6 (28,6)	2 (18,2)	8 (25,0)

PEACE	Pegzilarginase[a] (N = 21)	Placebo[a] (N = 11)	Gesamt (N = 32)
ATC-Klasse, n (%) Bevorzugter Name, n (%)			
Andere Antiepileptika	5 (23,8)	3 (27,3)	8 (25,0)
Keppra (Levetiracetam)	3 (14,3)	1 (9,1)	4 (12,5)
Andere Antihistaminika zur systemischen Anwendung	3 (14,3)	1 (9,1)	4 (12,5)
Desloratadin	2 (9,5)	1 (9,1)	3 (9,4)
Andere zentral wirkende Mittel	4 (19,0)	3 (27,3)	7 (21,9)
Baclofen	4 (19,0)	3 (27,3)	7 (21,9)
Andere Diätetika-Kombinationen	3 (14,3)	2 (18,2)	5 (15,6)
Kreatin	3 (14,3)	0	3 (9,4)
Andere Diätetika-Kombinationen	0	2 (18,2)	2 (6,3)
Andere virale Impfstoffe	6 (28,6)	4 (36,4)	10 (31,3)
Covid-19-Impfstoffe	2 (9,5)	2 (18,2)	4 (12,5)
Pfizer BioNTech Covid-19 Impfung	1 (4,8)	2 (18,2)	3 (9,4)
Sars-Cov-2 Impfung	2 (9,5)	0	2 (6,3)
Penicilline mit erweitertem Wirkungsspektrum	2 (9,5)	3 (27,3)	5 (15,6)
Amoxicillin	1 (4,8)	3 (27,3)	4 (12,5)
Piperazin-Derivate	7 (33,3)	6 (54,5)	13 (40,6)
Cetirizin	6 (28,6)	5 (45,5)	11 (34,4)
Propionsäure-Derivate	7 (33,3)	3 (27,3)	10 (31,3)
Ibuprofen	4 (19,0)	3 (27,3)	7 (21,9)
Protonenpumpenhemmer	1 (4,8)	5 (45,5)	6 (18,8)
Lansoprazol	1 (4,8)	2 (18,2)	3 (9,4)

PEACE	**Pegzilarginase[a] (N = 21)**	**Placebo[a] (N = 11)**	**Gesamt (N = 32)**
ATC-Klasse, n (%) Bevorzugter Name, n (%)			
Omeprazol	0	2 (18,2)	2 (6,3)
Cephalosporine der 2, Generation	0	2 (18,2)	2 (6,3)
Cefoxitin	0	2 (18,2)	2 (6,3)
Serotonin-5HT3-Rezeptorantagonisten	0	4 (36,4)	4 (12,5)
Ondansetron	0	3 (27,3)	3 (9,4)
Lösungen zur parenteralen Ernährung	5 (23,8)	5 (45,5)	10 (31,3)
Dextrose	2 (9,5)	2 (18,2)	4 (12,5)
Glucose	2 (9,5)	1 (9,1)	3 (9,4)
SMOFlipid	2 (9,5)	1 (9,1)	3 (9,4)
Lösungen zur parenteralen Ernährung	2 (9,5)	1 (9,1)	3 (9,4)
Substituierte Alkylamine	3 (14,3)	2 (18,2)	5 (15,6)
Chlorphenamin	3 (14,3)	2 (18,2)	5 (15,6)
Sonstige Mittel für das alimentäre System und den Stoffwechsel	20 (95,2)	9 (81,8)	29 (90,6)
Buphenyl	2 (9,5)	1 (9,1)	3 (9,4)
Pheburane	3 (14,3)	0	3 (9,4)
Ravicti	10 (47,6)	5 (45,5)	15 (46,9)
Natriumbenzoat	10 (47,6)	5 (45,5)	15 (46,9)
Natriumphenylbutyrat	2 (9,5)	2 (18,2)	4 (12,5)
Vitamin D und Analoga	10 (47,6)	3 (27,3)	13 (40,6)
Colecalciferol	3 (14,3)	1 (9,1)	4 (12,5)
Uvedose	3 (14,3)	1 (9,1)	4 (12,5)

PEACE	**Pegzilarginase[a] (N = 21)**	**Placebo[a] (N = 11)**	**Gesamt (N = 32)**
ATC-Klasse, n (%)			
Bevorzugter Name, n (%)			

ARG1-D: *Arginase-1 Deficiency*, ATC: *Anatomical Therapeutic Chemical*, IDM: *Individual Disease Management*, WHO*: World Health Organization*

a) In Kombination mit IDM. IDM umfasst u. a. diätetische Proteinrestriktion, ggf. die Supplementierung essenzieller Aminosäuren und Vitamine sowie die symptomatische Behandlung der zahlreichen Komplikationen des ARG1-D, was ggf. auch eine medikamentöse Therapie mit Stickstoff-Fängern einschließt.

Begleitmedikation wurden mit Hilfe des *WHO Drug Dictionary* kodiert und nach *ATC-Code* zusammengefasst. Sofern verfügbar, wurde der 4-stellige ATC-Code verwendet, andernfalls wurde der nächste hierarchisch niedrigere ATC-Code verwendet. Als Preferred Name wurde der aktive Wirkstoff verwendet. Falls der aktive Wirkstoff nicht genannt wurde und bei Arzneimitteln mit mehr als einem aktiven Wirkstoff wurde der Handelsname verwendet

4.3 Angabe des Endwertes inklusive Standardabweichung für alle Verlaufsbeobachtungen

4.3.1 Arginin-Konzentration im Plasma

Pegzilarginase[a]					Placebo[a]				Behandlungseffekt Pegzilarginase[a] vs. Placebo[a]	
PEACE	**N**	**Baseline-GMW (Log-Skala SD[b])**	**Woche 24-GMW (Log-Skala SD[b])**	**Woche 24-GMW/ Baseline-GMW (Log-Skala SD[b])**	**N**	**Baseline-GMW (Log-Skala SD[b])**	**Woche 24-GMW (Log-Skala SD[b])**	**Woche 24-GMW/ Baseline-GMW (Log-Skala SD[b])**	**GLSMR[c] [95-%-KI] p-Wert**	**SMD[b] gemäß Hedges‘ g [95-%-KI]**
Arginin	21	354,00 (0,261)	86,37 (0,471)	0,24 (0,492)	11	464,74 (0,188)	426,52 (0,270)	0,92 (0,315)	0,23 [0,16; 0,33] **<0,0001**	0,04 [0,01; 0,12]

ARG1-D: *Arginase-1 Deficiency*, GMW: Geometrischer Mittelwert, IDM: *Individual Disease Management*, KI: Konfidenzintervall, MMRM: *Mixed Model for Repeated Measurements*, N: Anzahl ausgewerteter Patienten, SD: *Standard Deviation*, SMD: Standardisierte Mittelwertdifferenzen, GLSMR: *Geometric Least Squares Mean Ratio* (Pegzilarginase/Placebo),

a) In Kombination mit IDM. IDM umfasst u. a. diätetische Proteinrestriktion, evtl. die Supplementierung essenzieller Aminosäuren und Vitamine sowie die symptomatische Behandlung der zahlreichen Komplikationen des ARG1-D, was ggf. auch eine medikamentöse Therapie mit Stickstoff-Fängern einschließt.

b) SD und SMD wurden auf Basis der logarithmierten Daten berechnet.

c) Es wurde ein MMRM mit einer unstrukturierten Kovarianzmatrix verwendet. Studienvisite, randomisierter Studienarm sowie die Interaktion zwischen Studienvisite und randomisiertem Studienarm wurden als feste Effekte und der Baseline-Wert als Kovariate berücksichtigt.

4.3.2 GC-Konzentration im Plasma

	Pegzilarginase[a]				Placebo[a]				Behandlungseffekt Pegzilarginase[a] vs. Placebo[a]	
PEACE	**N**	**Baseline-GMW (Log-Skala SD[b])**	**Woche 24-GMW (Log-Skala SD[b])**	**Woche 24-GMW/ Baseline-GMW (Log-Skala SD[b])**	**N**	**Baseline-GMW (Log-Skala SD[b])**	**Woche 24-GMW (Log-Skala SD[b])**	**Woche 24-GMW/ Baseline-GMW (Log-Skala SD[b])**	**GLSMR[c] [95-%-KI] p-Wert**	**SMD[b] gemäß Hedges‘ g [95-%-KI]**
ArgA	21	2,42 (0,430)	0,75 (0,597)	0,31 (0,502)	11	3,22 (0,405)	3,16 (0,384)	0,98 (0,217)	0,30 [0,22; 0,43] **<0,0001**	0,07 [0,03; 0,20]
GAA	21	3,42 (0,628)	1,66 (0,469)	0,48 (0,657)	11	3,58 (0,489)	3,67 (0,484)	1,02 (0,249)	0,47 [0,32; 0,68] **0,0003**	0,22 [0,10; 0,51]
GVA	21	4,49 (0,461)	1,33 (0,609)	0,30 (0,561)	11	5,39 (0,450)	4,80 (0,404)	0,89 (0,306)	0,32 [0,22; 0,45] **<0,0001**	0,10 [0,04; 0,25]
NAA	21	0,98 (0,661)	0,30 (0,753)	0,30 (0,719)	11	1,54 (0,641)	1,35 (0,547)	0,87 (0,434)	0,30 [0,19; 0,48] **<0,0001**	0,15 [0,06; 0,35]

ARG1-D: *Arginase-1 Deficiency*, ArgA: *Argininic Acid*, GAA: *Guanidinoacetic Acid*, GC: *Guanidino Compund*, GLSMR: *Geometric Least Squares Mean Ratio*, GMW: Geometrischer Mittelwert, GVA: *Alpha-Keto-Delta-Guanidinovaleric Acid*, IDM: *Individual Disease Management*, KI: Konfidenzintervall, MMRM: *Mixed Model for Repeated Measurements*, N: Anzahl ausgewerteter Patienten, NAA: N-Acetyl-L-Arginin, SD: *Standard Deviation*, SMD: Standardisierte Mittelwertdifferenzen,

a) In Kombination mit IDM. IDM umfasst u. a. diätetische Proteinrestriktion, evtl. die Supplementierung essenzieller Aminosäuren und Vitamine sowie die symptomatische Behandlung der zahlreichen Komplikationen des ARG1-D, was ggf. auch eine medikamentöse Therapie mit Stickstoff-Fängern einschließt.

b) SD und SMD wurden auf Basis der logarithmierten Daten berechnet.

c) Es wurde ein MMRM mit einer unstrukturierten Kovarianzmatrix verwendet. Studienvisite, randomisierter Studienarm sowie die Interaktion zwischen Studienvisite und randomisiertem Studienarm wurden als feste Effekte und der Baseline-Wert als Kovariate berücksichtigt.

4.3.3 Ammoniak-Konzentration im Plasma

	Pegzilarginase[a]				Placebo[a]				Behandlungseffekt Pegzilarginase[a] vs. Placebo[a]	
PEACE	**N**	**Werte zu Baseline MW (SD)**	**Werte zu Woche 24 MW (SD)**	**Änderung gegenüber Baseline LSM (SE)**	**N**	**Werte zu Baseline MW (SD)**	**Werte zu Woche 24 MW (SD)**	**Änderung gegenüber Baseline LSM (SE)**	**LSMD (SE) [95-%-KI] p-Wert**	**SMD gemäß Hedges‘ g [95-%-KI]**
Ammoniak[b]	18	29,14 (19,948)	32,39 (16,723)	4,10 (24,173)	10	28,70 (17,591)	79,89 (164,843)	73,35 (31,602)	-69,25 (39,786) [-150,84; 12,34] 0,0930	-0,65 [-1,44; 0,14]

ARG1-D: *Arginase-1 Deficiency*, IDM: *Individual Disease Management*, KI: Konfidenzintervall, LSM: *Least Squares Mean*, LSMD: *Least Squares Mean Difference*, MMRM: *Mixed Models for Repeated Measures*, MW: Mittelwert, N: Anzahl ausgewerteter Patienten, SD: *Standard Deviation*, SE*: Standard Error*, SMD: Standardisierte Mittelwertdifferenz

a) In Kombination mit IDM. IDM umfasst u. a. diätetische Proteinrestriktion, evtl. die Supplementierung essenzieller Aminosäuren und Vitamine sowie die symptomatische Behandlung der zahlreichen Komplikationen des ARG1-D, was ggf. auch eine medikamentöse Therapie mit Stickstoff-Fängern einschließt.

b) Es wurde ein MMRM mit einer unstrukturierten Kovarianzmatrix verwendet. Studienvisite, randomisierter Studienarm sowie die Interaktion zwischen Studienvisite und randomisiertem Studienarm wurden als feste Effekte und der Baseline-Wert als Kovariate berücksichtigt.

4.3.4 2MWT

	Pegzilarginase[a]				Placebo[a]				Behandlungseffekt Pegzilarginase[a] vs. Placebo[a]	
PEACE	**N**	**Werte zu Baseline MW (SD)**	**Werte zu Woche 24 MW (SD)**	**Änderung gegenüber Baseline LSM (SE)**	**N**	**Werte zu Baseline MW (SD)**	**Werte zu Woche 24 MW (SD)**	**Änderung gegenüber Baseline LSM (SE)**	**LSMD (SE) [95-%-KI] p-Wert**	**SMD gemäß Hedges‘ g [95-%-KI]**
2MWT[b]	19	109,00 (55,765)	115,85 (51,809)	7,44 (6,035)	10	99,91 (49,003)	102,30 (51,097)	1,92 (8,335)	5,52 (10,295) [-15,64; 26,69] 0,5961	0,20 [-0,57; 0,97]

2MWT: *2-Minute Walking Test*, ARG1-D: *Arginase-1 Deficiency*, IDM: *Individual Disease Management*, KI: Konfidenzintervall, LSM: *Least Squares Mean*, LSMD: *LSM Difference*, MMRM: *Mixed Models for Repeated Measures*, MW: Mittelwert, N: Anzahl ausgewerteter Patienten, SD: *Standard Deviation*, SE*: Standard Error*, SMD: Standardisierte Mittelwertdifferenz

a) In Kombination mit IDM. IDM umfasst u. a. diätetische Proteinrestriktion, evtl. die Supplementierung essenzieller Aminosäuren und Vitamine sowie die symptomatische Behandlung der zahlreichen Komplikationen des ARG1-D, was ggf. auch eine medikamentöse Therapie mit Stickstoff-Fängern einschließt.

b) Es wurde ein MMRM mit einer unstrukturierten Kovarianzmatrix verwendet. Studienvisite, randomisierter Studienarm sowie die Interaktion zwischen Studienvisite und randomisiertem Studienarm wurden als feste Effekte und der Baseline-Wert als Kovariate berücksichtigt.

4.3.5 GMFM

	Pegzilarginase[a]				Placebo[a]				Behandlungseffekt Pegzilarginase[a] vs. Placebo[a]	
PEACE	**N**	**Werte zu Baseline MW (SD)**	**Werte zu Woche 24 MW (SD)**	**Änderung gegenüber Baseline LSM (SE)**	**N**	**Werte zu Baseline MW (SD)**	**Werte zu Woche 24 MW (SD)**	**Änderung gegenüber Baseline LSM (SE)**	**LSMD (SE) [95-%-KI] p-Wert**	**SMD gemäß Hedges' g [95-%-KI]**
Hauptanalyse[b]										
GMFM-D	20	28,05 (9,610)	30,45 (10,092)	2,70 (0,808)	11	26,82 (14,764)	28,18 (13,280)	1,28 (1,091)	1,42 (1,358) [-1,36; 4,20] 0,3037	0,38 [-0,37; 1,12]
GMFM-E	20	48,33 (19,931)	51,95 (21,271)	4,20 (1,641)	11	46,45 (24,562)	46,09 (25,712)	-0,37 (2,215)	4,57 (2,755) [-1,08; 10,21] 0,1087	0,60 [-0,16; 1,35]
Sensitivitätsanalyse[c]										
GMFM-D	20	28,05 (9,610)	30,45 (10,092)	2,70 (0,870)	10	29,50 (12,421)	29,90 (12,644)	0,40 (0,322)	2,30 (0,929) [0,38; 4,22] **0,0208**	Nicht interpretierbar[d] 0,66 [-0,12; 1,44]
GMFM-E	20	48,33 (19,931)	51,95 (21,271)	4,21 (1,672)	10	50,20 (22,335)	49,60 (24,167)	-0,60 (2,359)	4,81 (2,893) [-1,12; 10,75] 0,1077	0,62 [-0,16; 1,39]

ARG1-D: *Arginase-1 Deficiency*, GMFCS: *Gross Motor Function Classification System*, GMFM: *Gross Motor Function Measure-88;* IDM: *Individual Disease Management*, KI: Konfidenzintervall, LSM: *Least Squares Mean*, LSMD: *Least Squares Mean Difference*, MMRM: *Mixed Models for Repeated Measures*, MW: Mittelwert, N: Anzahl ausgewerteter Patienten, SD: *Standard Deviation*, SE*: Standard Error*, SMD: Standardisierte Mittelwertdifferenz

a) In Kombination mit IDM. IDM umfasst u. a. diätetische Proteinrestriktion, evtl. die Supplementierung essenzieller Aminosäuren und Vitamine sowie die symptomatische Behandlung der zahlreichen Komplikationen des ARG1-D, was ggf. auch eine medikamentöse Therapie mit Stickstoff-Fängern einschließt.

b) Es wurde ein MMRM mit einer unstrukturierten Kovarianzmatrix verwendet. Studienvisite, randomisierter Studienarm sowie die Interaktion zwischen Studienvisite und randomisiertem Studienarm wurden als feste Effekte und der Baseline-Wert als Kovariate berücksichtigt.

c) Für einen Patienten wurde kein Baseline-Wert für den GMFM-D erhoben, jedoch als Wert irrtümlicherweise „0" eingetragen und beim GMFM-E ein unvollständig ausgefüllter Fragebogen zu Baseline wie ein vollständig ausgefüllter Fragebogen ausgewertet. Diese „0" bzw. der unvollständig ausgefüllte Fragebogen wurde für die Sensitivitätsanalyse dementsprechend zu einem fehlenden Wert korrigiert und die Messwerte dieses Patienten nicht berücksichtigt. Die Analyse mittels Levene Test zeigte, dass beim GMFM-D die Varianzen zwischen den Studienarmen ungleich sind (p-Wert = 0,0217). Dementsprechend wurde das MMRM angepasst, um diesen Effekt adäquat zu berücksichtigen. Hierfür

wurden die Varianzen im MMRM separat geschätzt. Für den GMFM-E wird in der Sensitivitätsanalyse dasselbe MMRM verwendet wie in der Hauptanalyse. Die Ergebnisse der Sensitivitätsanalyse sind folglich den Ergebnissen der Hauptanalyse vorzuziehen.

d) Die SMD gemäß Hedges‘ g ist als Effektschätzer für Behandlungsgruppen mit ungleichen Varianzen ungeeignet, da durch die Standardisierung mittels gepoolter Standardabweichung jegliche inhärenten Varianzunterschiede verdeckt werden [119]. Die SMD sollte dementsprechend nicht interpretiert werden und wird nur aus Gründen der formalen Vollständigkeit dargestellt.

4.3.6 FMS

Pegzilarginase[a]					Placebo[a]				Behandlungseffekt Pegzilarginase[a] vs. Placebo[a]	
PEACE	**N**	**Werte zu Baseline MW (SD)**	**Werte zu Woche 24 MW (SD)**	**Änderung gegenüber Baseline LSM (SE)**	**N**	**Werte zu Baseline MW (SD)**	**Werte zu Woche 24 MW (SD)**	**Änderung gegenüber Baseline LSM (SE)**	**LSMD (SE) [95-%-KI] p-Wert**	**SMD gemäß Hedges‘ g [95-%-KI]**
FMS-5[b]	20	5,15 (1,387)	5,20 (1,399)	0,05 (0,118)	11	4,82 (1,722)	4,73 (1,849)	-0,10 (0,160)	0,15 (0,199) [-0,25; 0,56] 0,4434	0,28 [-0,46; 1,02]
FMS-50[b]	19	5,00 (1,491)	5,15 (1,531)	0,22 (0,139)	11	4,55 (1,809)	4,64 (1,804)	0,07 (0,183)	0,15 (0,231) [-0,33; 0,62] 0,5301	0,23 [-0,51; 0,98]
FMS-500[b]	19	4,58 (1,677)	4,42 (1,895)	0,05 (0,074)	11	3,73 (2,240)	3,91 (2,343)	0,19 (0,096)	-0,14 (0,123) [-0,40; 0,11] 0,2515	-0,43 [-1,19; 0,33]

ARG1-D: *Arginase-1 Deficiency*, FMS: *Functional Mobility Scale*, IDM: *Individual Disease Management*, KI: Konfidenzintervall, LSM: *Least Squares Mean*, LSMD: *Least Squares Mean Difference*, MMRM: *Mixed Models for Repeated Measures*, MW: Mittelwert, N: Anzahl ausgewerteter Patienten, SD: *Standard Deviation*, SE*: Standard Error*, SMD: Standardisierte Mittelwertdifferenz

a) In Kombination mit IDM. IDM umfasst u. a. diätetische Proteinrestriktion, evtl. die Supplementierung essenzieller Aminosäuren und Vitamine sowie die symptomatische Behandlung der zahlreichen Komplikationen des ARG1-D, was ggf. auch eine medikamentöse Therapie mit Stickstoff-Fängern einschließt.

b) Für das MMRM wurde eine unstrukturierte Kovarianzmatrix verwendet. Studienvisite, randomisierter Studienarm sowie die Interaktion zwischen Studienvisite und randomisiertem Studienarm wurden als feste Effekte und der Baseline-Wert als Kovariate berücksichtigt.

4.3.7 GFAQ

Pegzilarginase[a]					Placebo[a]				Behandlungseffekt Pegzilarginase[a] vs. Placebo[a]	
PEACE	**N**	**Werte zu Baseline MW (SD)**	**Werte zu Woche 24**	**Änderung gegenüber Baseline LSM (SE)**	**N**	**Werte zu Baseline MW (SD)**	**Werte zu Woche 24**	**Änderung gegenüber Baseline LSM (SE)**	**LSMD (SE) [95-%-KI] p-Wert**	**SMD gemäß Hedges' g [95-%-KI]**
GFAQ[b]	20	7,90 (2,047)	7,95 (2,259)	0,10 (0,187)	11	7,45 (2,622)	7,18 (2,483)	-0,28 (0,254)	0,39 (0,316) [-0,26; 1,03] 0,2322	0,44 [-0,30; 1,18]

ARG1-D: *Arginase-1 Deficiency*, GFAQ: *Gillette Functional Assessment Questionnaire*, IDM: *Individual Disease Management*, KI: Konfidenzintervall, LSM: *Least Squares Mean*, LSMD: *Least Squares Mean Difference*, MMRM: *Mixed Models for Repeated Measures*, MW: Mittelwert, N: Anzahl ausgewerteter Patienten, SD: *Standard Deviation*, SE*: Standard Error*, SMD: Standardisierte Mittelwertdifferenz

a) In Kombination mit IDM. IDM umfasst u. a. diätetische Proteinrestriktion, evtl. die Supplementierung essenzieller Aminosäuren und Vitamine sowie die symptomatische Behandlung der zahlreichen Komplikationen des ARG1-D, was ggf. auch eine medikamentöse Therapie mit Stickstoff-Fängern einschließt.

b) Für das MMRM wurde eine unstrukturierte Kovarianzmatrix verwendet. Studienvisite, randomisierter Studienarm sowie die Interaktion zwischen Studienvisite und randomisiertem Studienarm wurden als feste Effekte und der Baseline-Wert als Kovariate berücksichtigt.

4.3.8 VABS-II

Pegzilarginase[a]					Placebo[a]				Behandlungseffekt Pegzilarginase[a] vs. Placebo[a]	
PEACE	**N**	**Werte zu Baseline MW (SD)**	**Werte zu Woche 24 MW (SD)**	**Änderung gegenüber Baseline LSM (SE)**	**N**	**Werte zu Baseline MW (SD)**	**Werte zu Woche 24 MW (SD)**	**Änderung gegenüber Baseline LSM (SE)**	**LSMD (SE) [95-%-KI] p-Wert**	**SMD gemäß Hedges‘ g [95-%-KI]**
Hauptanalysen[b]										
Kommunikation	20	71,45 (21,271)	69,10 (22,613)	-2,50 (1,516)	11	73,09 (28,655)	68,36 (22,473)	-4,74 (2,041)	2,24 (2,542) [-2,97; 7,45] 0,3858	0,32 [-0,42; 1,06]
Alltagskompetenz	20	72,05 (23,440)	70,95 (23,228)	-0,96 (1,902)	11	61,36 (20,588)	60,55 (21,575)	-1,22 (2,611)	0,25 (3,263) [-6,43; 6,93] 0,9390	0,03 [-0,71; 0,76]
Sozialisierung	19	82,84 (24,160)	77,30 (22,077)	-3,47 (2,547)	11	62,00 (19,261)	61,82 (16,185)	-3,00 (3,472)	-0,47 (4,480) [-9,65; 8,71] 0,9171	-0,04 [-0,78; 0,70]
Motorische Fähigkeiten	7	61,67 (37,487)	83,25 (47,334)	21,30 (24,475)	2	95,80 (56,367)	76,50 (24,749)	5,32 (55,494)	15,99 (60,667) [-133,28; 165,25] 0,8012	0,20 [-1,38; 1,77]
ABCS	18	71,55 (24,341)	76,22 (15,698)	1,56 (2,490)	10	67,27 (15,100)	66,70 (10,404)	-3,38 (3,433)	4,94 (4,247) [-3,81; 13,69] 0,2557	0,44 [-0,34; 1,22]
Sensitivitätsanalyse[b, c]										
ABCS	19	71,55 (24,341)	73,26 (19,977)	1,71 (2,526)	11	67,27 (15,100)	65,73 (10,384)	-3,08 (3,338)	4,79 (4,193) [-3,81; 13,39] 0,2630	0,42 [-0,34; 1,17]
Sensitivitätsanalyse[c,]										
Motorische Fähigkeiten	6	69,38 (31,541)	71,00 (26,952)	-5,54 (3,310)	2	71,00 (11,662)	76,50 (24,749)	5,75 (5,826)	-11,29 (6,710) [-27,40; 4,83] 0,1396	-1,12 [-2,84; 0,60]

ABCS: *Adaptive Behaviour Composite Score*, ARG1-D: *Arginase-1 Deficiency*, IDM: *Individual Disease Management*, KI: Konfidenzintervall, LSM: *Least Squares Mean*, LSMD: *Least Squares Mean Difference*, MMRM: *Mixed Models for Repeated Measures*, MW: Mittelwert, N: Anzahl ausgewerteter Patienten, SD: *Standard Deviation*, SE*: Standard Error*, SMD: Standardisierte Mittelwertdifferenz, VABS II: *Vineland Adaptive Behavior Scales, Second Edition*

c) In Kombination mit IDM. IDM umfasst u. a. diätetische Proteinrestriktion, evtl. die Supplementierung essenzieller Aminosäuren und Vitamine sowie die symptomatische Behandlung der zahlreichen Komplikationen des ARG1-D, was ggf. auch eine medikamentöse Therapie mit Stickstoff-Fängern einschließt.

d) Es wurde ein MMRM mit einer unstrukturierten Kovarianzmatrix verwendet. Studienvisite, randomisierter Studienarm sowie die Interaktion zwischen Studienvisite und randomisiertem Studienarm wurden als feste Effekte und der Baseline-Wert als Kovariate berücksichtigt

e) Unter Berücksichtigung von 2 Patienten, die bei der initialen Analyse des CSR irrtümlich für die Auswertung des ABCS nicht berücksichtigt wurden

f) In die Hauptanalyse gingen auch die Ergebnisse eines Patienten ein, dessen Messwerte durch Datenerhebungsfehler außerhalb der Skalenspannweite lagen, was nach Database Lock bemerkt wurde. Diese Daten wurden in der Sensitivitätsanalyse als fehlende Werte ersetzt.

4.3.9 CaGI-C und CGI-C

Pegzilarginase[a]				Placebo[a]			Behandlungseffekt Pegzilarginase[a] vs. Placebo[a]	
PEACE	**N**	**Eindruck der Änderung im Studienverlauf MW (SD)**	**Eindruck der Änderung im Studienverlaufb LSM (SE)**	**N**	**Eindruck der Änderung im Studienverlauf MW (SD)**	**Eindruck der Änderung im Studienverlaufb LSM (SE)**	**LSMD (SE) [95-%-KI] p-Wert**	**SMD gemäß Hedges‘ g [95-%-KI]**
CaGI-C								
Gehfähigkeit[c]	19	2,63 (0,684)	2,60 (0,179)	11	2,64 (0,924)	2,64 (0,236)	-0,03 (0,296) [-0,64; 0,57] 0,9092	-0,04 [-0,78; 0,70]
Hilfsmittel für die Fortbewegung[c]	18	2,67 (0,594)	2,67 (0,163)	10	2,40 (0,843)	2,40 (0,218)	0,27 (0,272) [-0,29; 0,83] 0,3366	0,37 [-0,41; 1,15]
Feinmotorik[c]	19	2,58 (0,507)	2,56 (0,132)	11	2,36 (0,674)	2,36 (0,173)	0,20 (0,218) [-0,25; 0,65] 0,3670	0,33 [-0,42; 1,08]
Grobmotorik[c]	19	2,68 (0,582)	2,65 (0,142)	11	2,55 (0,688)	2,55 (0,189)	0,11 (0,236) [-0,37; 0,59] 0,6486	0,17 [-0,58; 0,91]
Alltagskompetenz[c]	19	2,68 (0,582)	2,67 (0,143)	11	2,45 (0,688)	2,45 (0,188)	0,22 (0,236) [-0,26; 0,70] 0,3601	0,34 [-0,41; 1,09]
Kommunikation[c]	19	2,58 (0,692)	2,56 (0,162)	11	2,18 (0,751)	2,18 (0,215)	0,38 (0,269) [-0,17; 0,93] 0,1720	0,51 [-0,24; 1,26]
Sozialisierung[c]	19	2,74 (0,562)	2,74 (0,140)	11	2,55 (0,688)	2,55 (0,184)	0,19 (0,231) [-0,28; 0,66] 0,4183	0,30 [-0,45; 1,04]
Anpassungsfähigkeit an das Umfeld[c]	19	2,68 (0,671)	2,68 (0,155)	11	2,36 (0,674)	2,36 (0,203)	0,32 (0,255) [-0,20; 0,84] 0,2199	0,45 [-0,30; 1,21]

Pegzilarginase[a]				Placebo[a]			Behandlungseffekt Pegzilarginase[a] vs. Placebo[a]	
PEACE	**N**	**Eindruck der Änderung im Studienverlauf MW (SD)**	**Eindruck der Änderung im Studienverlaufb LSM (SE)**	**N**	**Eindruck der Änderung im Studienverlauf MW (SD)**	**Eindruck der Änderung im Studienverlaufb LSM (SE)**	**LSMD (SE) [95-%-KI] p-Wert**	**SMD gemäß Hedges‘ g [95-%-KI]**
CGI-C								
Gehfähigkeit[c]	18	2,67 (0,485)	2,67 (0,116)	8	2,63 (0,518)	2,64 (0,173)	0,03 (0,209) [-0,40; 0,46] 0,8991	0,05 [-0,78; 0,88]
Hilfsmittel für die Fortbewegung[c]	16	2,88 (0,342)	2,88 (0,072)	7	3,00 (0,000)	3,00 (0,111)	-0,12 (0,132) [-0,40; 0,15] 0,3683	-0,40 [-1,29; 0,50]

ARG1-D: *Arginase-1 Deficiency*, CaGI-C: *Caregiver Global Impressions of Change*, CGI-C: *Clinician Global Impressions of Change*, IDM: *Individual Disease Management*, KI: Konfidenzintervall, LSM: *Least Squares Mean*, LSMD: *Least Squares Mean Difference*, MMRM: *Mixed Models for Repeated Measures*, MW: Mittelwert, N: Anzahl ausgewerteter Patienten, SD: *Standard Deviation*, SE*: Standard Error*, SMD: Standardisierte Mittelwertdifferenz

a) In Kombination mit IDM. IDM umfasst u. a. diätetische Proteinrestriktion, evtl. die Supplementierung essenzieller Aminosäuren und Vitamine sowie die symptomatische Behandlung der zahlreichen Komplikationen des ARG1-D, was ggf. auch eine medikamentöse Therapie mit Stickstoff-Fängern einschließt.

b) Der CaGI-C und CGI-C wird per Definition nicht zu Baseline erhoben.

c) Es wurde ein MMRM mit einer unstrukturierten Kovarianzmatrix verwendet. Studienvisite, randomisierter Studienarm sowie die Interaktion zwischen Studienvisite und randomisiertem Studienarm wurden als feste Effekte berücksichtigt.

4.3.10 CaGI-S und CGI-S

Pegzilarginase[a]					Placebo[a]				Behandlungseffekt Pegzilarginase[a] vs. Placebo[a]	
PEACE	**N**	**Werte zu Baseline MW (SD)**	**Werte zu Woche 24 MW (SD)**	**Änderung gegenüber Baseline LSM (SE)**	**N**	**Werte zu Baseline MW (SD)**	**Werte zu Woche 24 MW (SD)**	**Änderung gegenüber Baseline LSM (SE)**	**LSMD (SE) [95-%-KI] p-Wert**	**SMD gemäß Hedges' g [95-%-KI]**
CaGI-S: Hauptanalysen[b]										
Gehfähigkeit	14	2,28 (1,274)	2,19 (1,276)	-0,49 (0,164)	7	2,88 (1,246)	2,89 (1,054)	0,14 (0,237)	-0,63 (0,290) [-1,24; -0,03] **0,0420**	-0,96 [-1,92; -0,00]
Hilfsmittel für die Fortbewegung	13	2,00 (1,458)	2,06 (1,340)	-0,34 (0,306)	6	3,00 (1,528)	2,67 (1,581)	0,44 (0,451)	-0,78 (0,548) [-1,94; 0,37] 0,1709	-0,66 [-1,65; 0,33]
Feinmotorik	13	2,11 (1,183)	2,07 (1,033)	-0,31 (0,286)	7	2,50 (0,926)	2,67 (1,500)	0,07 (0,390)	-0,38 (0,484) [-1,40; 0,64] 0,4432	-0,34 [-1,27; 0,58]
Grobmotorik	14	2,06 (1,162)	2,44 (1,365)	-0,03 (0,292)	7	3,38 (1,061)	3,33 (1,225)	0,45 (0,437)	-0,48 (0,540) [-1,60; 0,65] 0,3878	-0,40 [-1,32; 0,51]
Alltagskompetenz	14	2,06 (1,259)	2,06 (1,340)	-0,15 (0,280)	6	2,88 (1,458)	2,13 (1,126)	-0,14 (0,425)	-0,01 (0,511) [-1,09; 1,07] 0,9839	-0,01 [-0,97; 0,95]
Kommunikation	14	2,00 (1,328)	2,13 (1,204)	-0,21 (0,179)	6	3,00 (1,773)	2,25 (1,389)	-0,57 (0,273)	0,36 (0,330) [-0,35; 1,07] 0,2920	0,49 [-0,48; 1,46]
Sozialisierung	14	1,78 (0,878)	1,88 (1,025)	-0,24 (0,212)	7	2,88 (1,356)	2,56 (1,424)	0,24 (0,311)	-0,48 (0,387) [-1,30; 0,34] 0,2309	-0,56 [-1,48; 0,37]
Anpassungsfähigkeit an das Umfeld	14	1,78 (1,060)	1,88 (1,204)	-0,27 (0,269)	7	2,75 (1,669)	2,67 (1,323)	0,27 (0,390)	-0,53 (0,486) [-1,56; 0,49] 0,2874	-0,49 [-1,41; 0,43]

Pegzilarginase[a]					Placebo[a]				Behandlungseffekt Pegzilarginase[a] vs. Placebo[a]	
PEACE	**N**	**Werte zu Baseline MW (SD)**	**Werte zu Woche 24 MW (SD)**	**Änderung gegenüber Baseline LSM (SE)**	**N**	**Werte zu Baseline MW (SD)**	**Werte zu Woche 24 MW (SD)**	**Änderung gegenüber Baseline LSM (SE)**	**LSMD (SE) [95-%-KI] p-Wert**	**SMD gemäß Hedges‘ g [95-%-KI]**
CaGI-S: Sensitivitätsanalyse[c]										
Sozialisierung	14	1,78 (0,878)	1,88 (1,025)	-0,21 (0,142)	7	2,88 (1,356)	2,56 (1,424)	0,17 (0,430)	-0,38 (0,461) [-1,45; 0,68] 0,4322	Nicht interpretierbar[d] -0,41 [-1,33; 0,50]
CGI-S										
Gehfähigkeit[b]	15	2,61 (1,650)	2,87 (1,642)	-0,06 (0,291)	7	2,86 (1,464)	3,00 (1,309)	-0,15 (0,422)	0,09 (0,513) [-0,99; 1,16] 0,8691	0,07 [-0,83; 0,97]
Hilfsmittel für die Fortbewegung[b]	14	2,33 (1,680)	2,86 (1,748)	0,24 (0,277)	7	2,29 (1,604)	2,38 (1,408)	-0,17 (0,392)	0,42 (0,480) [-0,59; 1,42] 0,3943	0,38 [-0,54; 1,29]

ARG1-D: *Arginase-1 Deficiency*, CaGI-S: *Caregiver Global Impressions of Severity*, CGI-S: *Clinician Global Impressions of Severity*, IDM: *Individual Disease Management*, KI: Konfidenzintervall, LSM: *Least Squares Mean*, LSMD: *Least Squares Mean Difference*, MMRM: *Mixed Models for Repeated Measures*, MW: Mittelwert, N: Anzahl ausgewerteter Patienten, SD: *Standard Deviation*, SE*: Standard Error*, SMD: Standardisierte Mittelwertdifferenz,

a) In Kombination mit IDM. IDM umfasst u. a. diätetische Proteinrestriktion, evtl. die Supplementierung essenzieller Aminosäuren und Vitamine sowie die symptomatische Behandlung der zahlreichen Komplikationen des ARG1-D, was ggf. auch eine medikamentöse Therapie mit Stickstoff-Fängern einschließt.

b) Es wurde ein MMRM mit einer unstrukturierten Kovarianzmatrix verwendet. Studienvisite, randomisierter Studienarm sowie die Interaktion zwischen Studienvisite und randomisiertem Studienarm wurden als feste Effekte und der Baseline-Wert als Kovariate berücksichtigt.

c) Die Analyse mittels Levene Test zeigte, dass die Varianzen zwischen den Studienarmen ungleich sind (p-Wert = 0,0347). Dementsprechend wurde das MMRM angepasst, um diesen Effekt adäquat zu berücksichtigen. Hierfür wurden die Varianzen im MMRM separat geschätzt.

d) Die SMD gemäß Hedges‘ g ist als Effektschätzer für Behandlungsgruppen mit ungleichen Varianzen ungeeignet, da durch die Standardisierung mittels gepoolter Standardabweichung jegliche inhärenten Varianzunterschiede verdeckt werden. Die SMD sollte dementsprechend nicht interpretiert werden und wird nur aus Gründen der formalen Vollständigkeit dargestellt.

4.3.11 9HPT

Pegzilarginase[a]					Placebo[a]				Behandlungseffekt Pegzilarginase[a] vs. Placebo[a]	
PEACE	**N**	**Werte zu Baseline MW (SD)**	**Werte zu Woche 24 MW (SD)**	**Änderung gegenüber Baseline LSM (SE)**	**N**	**Werte zu Baseline MW (SD)**	**Werte zu Woche 24 MW (SD)**	**Änderung gegenüber Baseline LSM (SE)**	**LSMD (SE) [95-%-KI] p-Wert**	**SMD gemäß Hedges' g [95-%-KI]**
Hauptanalysen										
Dominante Hand[b]	15	2,21 (2,392)	3,65 (3,436)	-2,76 (0,92)	11	12,13 (27,566)	4,15 (3,803)	-2,40 (1,11)	-0,36 (1,46) [-3,36; 2,64] 0,8065	0,49 [-0,30; 1,28]
Nicht-dominante Hand[b]	15	3,08 (3,545)	4,96 (4,477)	-3,89 (1,33)	11	16,91 (36,359)	6,11 (5,931)	-2,57 (1,63)	-1,32 (2,14) [-5,74; 3,10] 0,5446	0,50 [-0,29; 1,29]
Sensitivitätsanalysen[c]										
Dominante Hand[b]	15	2,21 (2,392)	3,65 (3,436)	0,96 (0,79)	9	4,25 (3,776)	4,84 (3,869)	0,99 (1,04)	-0,03 (1,32) [-2,77; 2,71] 0,9813	0,14 [-0,69; 0,96]
Nicht-dominante Hand[b]	15	3,08 (3,545)	4,96 (4,477)	1,53 (0,76)	9	6,76 (6,311)	7,09 (6,145)	0,50 (1,02)	1,03 (1,30) [-1,67; 3,74] 0,4358	0,41 [-0,42; 1,25]

9HPT: 9-Hole Pegboard Test, ARG1-D: *Arginase-1 Deficiency*, IDM: *Individual Disease Management*, KI: Konfidenzintervall, LSM: *Least Squares Mean*, LSMD: *Least Squares Mean Difference*, MMRM: *Mixed Models for Repeated Measures*, MW: Mittelwert, N: Anzahl ausgewerteter Patienten, SD: *Standard Deviation*, SE*: Standard Error*, SMD: Standardisierte Mittelwertdifferenz,

a) In Kombination mit IDM. IDM umfasst u. a. diätetische Proteinrestriktion, evtl. die Supplementierung essenzieller Aminosäuren und Vitamine sowie die symptomatische Behandlung der zahlreichen Komplikationen des ARG1-D, was ggf. auch eine medikamentöse Therapie mit Stickstoff-Fängern einschließt.

b) Es wurde ein MMRM mit einer unstrukturierten Kovarianzmatrix verwendet. Studienvisite, randomisierter Studienarm sowie die Interaktion zwischen Studienvisite und randomisiertem Studienarm wurden als feste Effekte und der Baseline-Wert als Kovariate berücksichtigt.

c) Daten von 2 Patienten mit bekannten Datenerhebungsfehlern werden als fehlende Werte ersetzt

In die Hauptanalyse gingen auch die Ergebnisse von 2 Patienten ein, deren Messwerte durch bekannte Datenerhebungsfehler verzerrt sind. Diese Patienten wurden dementsprechend in einer Sensitivitätsanalyse ausgeschlossen. Die Ergebnisse der Sensitivitätsanalyse sind daher den Ergebnissen der Hauptanalyse vorzuziehen.

4.3.12 WIS

Pegzilarginase[a]					Placebo[a]				Behandlungseffekt Pegzilarginase[a] vs. Placebo[a]	
PEACE	**N**	**Werte zu Baseline MW (SD)**	**Werte zu Woche 24 MW (SD)**	**Änderung gegenüber Baseline LSM (SE)**	**N**	**Werte zu Baseline MW (SD)**	**Werte zu Woche 24 MW (SD)**	**Änderung gegenüber Baseline LSM (SE)**	**LSMD (SE) [95-%-KI] p-Wert**	**SMD gemäß Hedges‘ g [95-%-KI]**
Hauptanalysen										
FSIQ[b]	11	62,27 (14,587)	68,29 (15,910)	3,62 (1,657)	3	59,83 (21,931)	69,17 (21,028)	5,05 (3,199)	-1,43 (3,620) [-9,40; 6,54] 0,7004	-0,23 [-1,51; 1,05]
Sensitivitätsanalysen[c]										
FSIQ[b]	10	62,57 (15,088)	68,33 (17,249)	3,30 (1,843)	2	61,75 (25,237)	68,40 (23,416)	6,52 (4,151)	-3,22 (4,555) [-13,53; 7,08] 0,4970	-0,48 [-2,01; 1,05]

ARG1-D: *Arginase-1 Deficiency*, FSIQ: *Full Scale Intelligence Quotient*, IDM: *Individual Disease Management*, KI: Konfidenzintervall, LSM: *Least Squares Mean*, LSMD: *Least Squares Mean Difference*, MMRM: *Mixed Models for Repeated Measures*, MW: Mittelwert, N: Anzahl ausgewerteter Patienten, SD: *Standard Deviation*, SE*: Standard Error*, SMD: Standardisierte Mittelwertdifferenz, *WIS: Wechsler Intelligence Scales*

a) In Kombination mit IDM. IDM umfasst u. a. diätetische Proteinrestriktion, evtl. die Supplementierung essenzieller Aminosäuren und Vitamine sowie die symptomatische Behandlung der zahlreichen Komplikationen des ARG1-D, was ggf. auch eine medikamentöse Therapie mit Stickstoff-Fängern einschließt.

b) Es wurde ein MMRM mit einer unstrukturierten Kovarianzmatrix verwendet. Studienvisite, randomisierter Studienarm sowie die Interaktion zwischen Studienvisite und randomisiertem Studienarm wurden als feste Effekte und der Baseline-Wert als Kovariate berücksichtigt.

c) Für die Sensitivitätsanalyse wurden 4 Patienten ausgeschlossen, deren Messwerte bei der Überprüfung durch einen externen Berater Unstimmigkeiten aufwiesen oder nicht überprüfbar waren.

4.3.13 PedsQL

Pegzilarginase[a]					Placebo[a]				Behandlungseffekt Pegzilarginase[a] vs. Placebo[a]	
PEACE	**N**	**Werte zu Baseline MW (SD)**	**Werte zu Woche 24 MW (SD)**	**Änderung gegenüber Baseline LSM (SE)**	**N**	**Werte zu Baseline MW (SD)**	**Werte zu Woche 24 MW (SD)**	**Änderung gegenüber Baseline LSM (SE)**	**LSMD (SE) [95-%-KI] p-Wert**	**SMD gemäß Hedges' g [95-%-KI]**
Hauptanalysen										
Physische Funktion	17	71,54 (23,479)	71,57 (21,300)	-1,28 (4,553)	8	66,33 (26,787)	55,47 (16,508)	-14,13 (6,770)	12,86 (8,196) [-4,16; 29,88] 0,1313	0,64 [-0,22; 1,50]
Emotionale Funktion	17	66,58 (23,866)	76,47 (19,427)	9,68 (3,767)	8	66,67 (20,616)	65,63 (24,266)	-3,14 (5,593)	12,82 (6,750) [-1,15; 26,78] 0,0702	0,78 [-0,09; 1,65]
Soziale Funktion	17	79,21 (18,125)	79,31 (16,699)	2,71 (3,481)	8	62,78 (22,654)	63,75 (23,107)	-6,54 (5,217)	9,25 (6,308) [-3,78; 22,27] 0,1557	0,61 [-0,25; 1,46]
Schulische Funktion	16	73,33 (21,494)	69,17 (18,679)	-6,70 (3,712)	8	54,44 (20,378)	50,63 (21,118)	-9,97 (5,345)	3,27 (6,676) [-10,48; 17,02] 0,6282	0,21 [-0,64; 1,06]
Gesamtscore	18	72,48 (16,037)	73,78 (15,206)	0,99 (2,598)	8	63,04 (20,393)	58,70 (17,333)	-9,26 (3,908)	10,25 (4,735) [0,49; 20,01] **0,0402**	0,88 [0,01; 1,75]
Summenwert der physischen Gesundheit	17	71,54 (23,479)	71,57 (21,300)	-1,28 (4,553)	8	66,33 (26,787)	55,47 (16,508)	-14,13 (6,770)	12,86 (8,196) [-4,16; 29,88] 0,1313	0,64 [-0,22; 1,50]
Summenwert der psychosozialen Gesundheit	17	72,60 (15,578)	75,51 (15,359)	2,94 (2,585)	8	61,30 (19,779)	60,43 (20,225)	-5,54 (3,873)	8,48 (4,690) [-1,20; 18,16] 0,0832	0,75 [-0,12; 1,62]

ARG1-D: *Arginase-1 Deficiency*, IDM: *Individual Disease Management*, KI: Konfidenzintervall, LSM: *Least Squares Mean*, LSMD: *Least Squares Mean Difference*, MMRM: *Mixed Models for Repeated Measures*, MW: Mittelwert, N: Anzahl ausgewerteter Patienten, PedsQL: *Pediatric Quality of Life Inventory*, SD: *Standard Deviation*, SE*: Standard Error*, SMD: Standardisierte Mittelwertdifferenz,

a) In Kombination mit IDM. IDM umfasst u. a. diätetische Proteinrestriktion, evtl. die Supplementierung essenzieller Aminosäuren und Vitamine sowie die symptomatische Behandlung der zahlreichen Komplikationen des ARG1-D, was ggf. auch eine medikamentöse Therapie mit Stickstoff-Fängern einschließt.

b) Es wurde ein MMRM mit einer unstrukturierten Kovarianzmatrix verwendet. Studienvisite, randomisierter Studienarm sowie die Interaktion zwischen Studienvisite und randomisiertem Studienarm wurden als feste Effekte und der Baseline-Wert als Kovariate berücksichtigt.

4.4 Ergänzende Responderanalysen

4.4.1 CaGI-C

4.4.1.1 CaGI-C ability to walk responders - any improvement

Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Week 12	n (%)	21 (100.00)	11 (100.00)
	Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
	Number of patients imputed as non-responders : n (%)	4 (19.05)	1 (9.09)
	Non-Responders [1]	17 (80.95)	8 (72.73)
	Responders	4 (19.05)	3 (27.27)
	OR (95% CI)	0.63 (0.11, 3.49)	
	RR (95% CI)	0.70 (0.19, 2.58)	
	RD % (95% CI)	-8.23 (-39.45, 23.00)	
	p-value – Fisher's Exact Test	0.6675	
Week 24	n (%)	21 (100.00)	11 (100.00)
	Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
	Number of patients imputed as non-responders : n (%)	2 (9.52)	0 (0.00)
	Non-Responders [1]	14 (66.67)	8 (72.73)
	Responders	7 (33.33)	3 (27.27)
	OR (95% CI)	1.33 (0.27, 6.65)	
	RR (95% CI)	1.22 (0.39, 3.82)	
	RD % (95% CI)	6.06 (-27.09, 39.21)	
	p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.

Program: t-qs-categ-cagic.sas
Table Generation: 11SEP2023 9:28:11 AM

4.4.1.2 CaGI-C dependance on assistive device responders - any improvement

Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Week 12	n (%)	21 (100.00)	11 (100.00)
	Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
	Number of patients imputed as non-responders : n (%)	6 (28.57)	2 (18.18)
	Non-Responders [1]	19 (90.48)	8 (72.73)
	Responders	2 (9.52)	3 (27.27)
	OR (95% CI)	0.28 (0.04, 2.01)	
	RR (95% CI)	0.35 (0.07, 1.79)	
	RD % (95% CI)	-17.75 (-46.91, 11.41)	
	p-value – Fisher's Exact Test	0.3098	
Week 24	n (%)	21 (100.00)	11 (100.00)
	Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
	Number of patients imputed as non-responders : n (%)	3 (14.29)	1 (9.09)
	Non-Responders [1]	16 (76.19)	7 (63.64)
	Responders	5 (23.81)	4 (36.36)
	OR (95% CI)	0.55 (0.11, 2.67)	
	RR (95% CI)	0.65 (0.22, 1.95)	
	RD % (95% CI)	-12.55 (-46.32, 21.21)	
	p-value – Fisher's Exact Test	0.6808	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-cagic.sas
Table Generation: 11SEP2023 9:28:17 AM

4.4.1.3 CaGI-C fine motor skills responders - any improvement

Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Week 12	n (%)	21 (100.00)	11 (100.00)
	Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
	Number of patients imputed as non-responders : n (%)	4 (19.05)	1 (9.09)
	Non-Responders [1]	17 (80.95)	8 (72.73)
	Responders	4 (19.05)	3 (27.27)
	OR (95% CI)	0.63 (0.11, 3.49)	
	RR (95% CI)	0.70 (0.19, 2.58)	
	RD % (95% CI)	-8.23 (-39.45, 23.00)	
	p-value – Fisher's Exact Test	0.6675	
Week 24	n (%)	21 (100.00)	11 (100.00)
	Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
	Number of patients imputed as non-responders : n (%)	2 (9.52)	0 (0.00)
	Non-Responders [1]	13 (61.90)	5 (45.45)
	Responders	8 (38.10)	6 (54.55)
	OR (95% CI)	0.51 (0.12, 2.25)	
	RR (95% CI)	0.70 (0.32, 1.50)	
	RD % (95% CI)	-16.45 (-52.47, 19.57)	
	p-value – Fisher's Exact Test	0.4651	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-cagic.sas
Table Generation: 11SEP2023 9:28:23 AM

4.4.1.4 CaGI-C gross motor skills responders - any improvement

Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Week 12	n (%)	21 (100.00)	11 (100.00)
	Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
	Number of patients imputed as non-responders : n (%)	4 (19.05)	1 (9.09)
	Non-Responders [1]	16 (76.19)	7 (63.64)
	Responders	5 (23.81)	4 (36.36)
	OR (95% CI)	0.55 (0.11, 2.67)	
	RR (95% CI)	0.65 (0.22, 1.95)	
	RD % (95% CI)	-12.55 (-46.32, 21.21)	
	p-value – Fisher's Exact Test	0.6808	
Week 24	n (%)	21 (100.00)	11 (100.00)
	Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
	Number of patients imputed as non-responders : n (%)	2 (9.52)	0 (0.00)
	Non-Responders [1]	16 (76.19)	7 (63.64)
	Responders	5 (23.81)	4 (36.36)
	OR (95% CI)	0.55 (0.11, 2.67)	
	RR (95% CI)	0.65 (0.22, 1.95)	
	RD % (95% CI)	-12.55 (-46.32, 21.21)	
	p-value – Fisher's Exact Test	0.6808	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-cagic.sas
Table Generation: 11SEP2023 9:28:29 AM

4.4.1.5 CaGI-C daily living skills responders - any improvement

Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Week 12	n (%)	21 (100.00)	11 (100.00)
	Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
	Number of patients imputed as non-responders : n (%)	4 (19.05)	1 (9.09)
	Non-Responders [1]	16 (76.19)	9 (81.82)
	Responders	5 (23.81)	2 (18.18)
	OR (95% CI)	1.41 (0.23, 8.78)	
	RR (95% CI)	1.31 (0.30, 5.69)	
	RD % (95% CI)	5.63 (-23.55, 34.81)	
	p-value – Fisher's Exact Test	1.0000	
Week 24	n (%)	21 (100.00)	11 (100.00)
	Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
	Number of patients imputed as non-responders : n (%)	2 (9.52)	0 (0.00)
	Non-Responders [1]	16 (76.19)	6 (54.55)
	Responders	5 (23.81)	5 (45.45)
	OR (95% CI)	0.38 (0.08, 1.78)	
	RR (95% CI)	0.52 (0.19, 1.43)	
	RD % (95% CI)	-21.65 (-56.25, 12.96)	
	p-value – Fisher's Exact Test	0.2515	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-cagic.sas
Table Generation: 11SEP2023 9:28:35 AM

4.4.1.6 CaGI-C communication skills responders - any improvement

Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Week 12	n (%)	21 (100.00)	11 (100.00)
	Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
	Number of patients imputed as non-responders : n (%)	4 (19.05)	1 (9.09)
	Non-Responders [1]	13 (61.90)	7 (63.64)
	Responders	8 (38.10)	4 (36.36)
	OR (95% CI)	1.08 (0.24, 4.88)	
	RR (95% CI)	1.05 (0.40, 2.72)	
	RD % (95% CI)	1.73 (-33.48, 36.94)	
	p-value – Fisher's Exact Test	1.0000	
Week 24	n (%)	21 (100.00)	11 (100.00)
	Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
	Number of patients imputed as non-responders : n (%)	2 (9.52)	0 (0.00)
	Non-Responders [1]	15 (71.43)	4 (36.36)
	Responders	6 (28.57)	7 (63.64)
	OR (95% CI)	0.23 (0.05, 1.08)	
	RR (95% CI)	0.45 (0.20, 1.01)	
	RD % (95% CI)	-35.06 (-69.44, -0.69)	
	p-value – Fisher's Exact Test	0.0721	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-cagic.sas
Table Generation: 11SEP2023 9:28:40 AM

4.4.1.7 CaGI-C socialization skills responders - any improvement

Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Week 12	n (%)	21 (100.00)	11 (100.00)
	Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
	Number of patients imputed as non-responders : n (%)	4 (19.05)	1 (9.09)
	Non-Responders [1]	15 (71.43)	8 (72.73)
	Responders	6 (28.57)	3 (27.27)
	OR (95% CI)	1.07 (0.21, 5.44)	
	RR (95% CI)	1.05 (0.32, 3.40)	
	RD % (95% CI)	1.30 (-31.35, 33.95)	
	p-value – Fisher's Exact Test	1.0000	
Week 24	n (%)	21 (100.00)	11 (100.00)
	Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
	Number of patients imputed as non-responders : n (%)	2 (9.52)	0 (0.00)
	Non-Responders [1]	17 (80.95)	7 (63.64)
	Responders	4 (19.05)	4 (36.36)
	OR (95% CI)	0.41 (0.08, 2.13)	
	RR (95% CI)	0.52 (0.16, 1.70)	
	RD % (95% CI)	-17.32 (-50.33, 15.70)	
	p-value – Fisher's Exact Test	0.3970	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-cagic.sas
Table Generation: 11SEP2023 9:28:46 AM

4.4.1.8 CaGI-C ability to adapt to environment responders - any improvement

Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Week 12	n (%)	21 (100,00)	11 (100,00)
	Number of patients with missing data: n (%)	0 (0,00)	0 (0,00)
	Number of patients imputed as non-responders : n (%)	4 (19,05)	1 (9,09)
	Non-Responders [1]	16 (76,19)	6 (54,55)
	Responders	5 (23,81)	5 (45,45)
	OR (95% CI)	0,38 (0,08; 1,78)	
	RR (95% CI)	0,52 (0,19; 1,43)	
	RD % (95% CI)	-21,65 (-56,25; 12,96)	
	p-value – Fisher's Exact Test	0,2515	
Week 24	n (%)	21 (100,00)	11 (100,00)
	Number of patients with missing data: n (%)	0 (0,00)	0 (0,00)
	Number of patients imputed as non-responders : n (%)	2 (9,52)	0 (0,00)
	Non-Responders [1]	15 (71,43)	5 (45,45)
	Responders	6 (28,57)	6 (54,55)
	OR (95% CI)	0,33 (0,07; 1,52)	
	RR (95% CI)	0,52 (0,22; 1,24)	
	RD % (95% CI)	-25,97 (-61,18; 9,23)	
	p-value – Fisher's Exact Test	0,2499	

Abbreviations: CI = Confidence Interval; N = number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio,
NOTE: The option 'Answer not selected' has been imputed as missing value,
[1] Non-Responder-Imputation (NRI) of missing values,
NOTE: Zero cell correction performed: in the event of zero cells; the correction value of 0,5 added to each cell frequency of the corresponding fourfold table,
Program: t-qs-categ-cagic,sas
Table Generation: 11SEP2023 9:28:53 AM

4.5 CGI-C

4.5.1 CGI-C ability to walk responders - any improvement

Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Week 12	n (%)	21 (100.00)	11 (100.00)
	Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
	Number of patients imputed as non-responders : n (%)	7 (33.33)	2 (18.18)
	Non-Responders [1]	19 (90.48)	9 (81.82)
	Responders	2 (9.52)	2 (18.18)
	OR (95% CI)	0.47 (0.06, 3.92)	
	RR (95% CI)	0.52 (0.08, 3.23)	
	RD % (95% CI)	-8.66 (-34.68, 17.36)	
	p-value – Fisher's Exact Test	0.5932	
Week 24	n (%)	21 (100.00)	11 (100.00)
	Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
	Number of patients imputed as non-responders : n (%)	3 (14.29)	3 (27.27)
	Non-Responders [1]	15 (71.43)	8 (72.73)
	Responders	6 (28.57)	3 (27.27)
	OR (95% CI)	1.07 (0.21, 5.44)	
	RR (95% CI)	1.05 (0.32, 3.40)	
	RD % (95% CI)	1.30 (-31.35, 33.95)	
	p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-cagic.sas
Table Generation: 11SEP2023 9:28:59 AM

4.5.2 CGI-C dependance on assistive device responders - any improvement

Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Week 12	n (%)	21 (100.00)	11 (100.00)
	Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
	Number of patients imputed as non-responders : n (%)	8 (38.10)	2 (18.18)
	Non-Responders [1]	20 (95.24)	9 (81.82)
	Responders	1 (4.76)	2 (18.18)
	OR (95% CI)	0.23 (0.02, 2.81)	
	RR (95% CI)	0.26 (0.03, 2.58)	
	RD % (95% CI)	-13.42 (-37.97, 11.13)	
	p-value – Fisher's Exact Test	0.2661	
Week 24	n (%)	21 (100.00)	11 (100.00)
	Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
	Number of patients imputed as non-responders : n (%)	5 (23.81)	4 (36.36)
	Non-Responders [1]	19 (90.48)	11 (100.00)
	Responders	2 (9.52)	0 (0.00)
	OR (95% CI)	2.95 (0.13, 66.95)	
	RR (95% CI)	2.73 (0.14, 52.30)	
	RD % (95% CI)	7.20 (-10.23, 24.62)	
	p-value – Fisher's Exact Test	0.5343	

Abbreviations: CI = Confidence Interval; N = number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-cagic.sas
Table Generation: 11SEP2023 9:29:04 AM

4.6 PedsQL

4.6.1 Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score (responders ≥ 15)

Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Week 12	n (%)	20 (100.00)	9 (100.00)
	Self-report: n (%)	10 (50.00)	4 (44.44)
	Parent Report: n (%)	9 (45.00)	4 (44.44)
	Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
	Number of patients imputed as non-responders: n (%)	1 (5.00)	1 (11.11)
	Non-Responders [1]	17 (85.00)	9 (100.00)
	Responders	3 (15.00)	0 (0.00)
	OR (95% CI)	3.80 (0.18, 81.59)	
	RR (95% CI)	3.33 (0.19, 58.55)	
	RD % (95% CI)	11.67 (-9.23, 32.56)	
	p-value – Fisher's Exact Test	0.5320	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Data Pooled Across all Age groups
Table Generation: 11SEP2023 12:10:18 PM
Program: t-qs-categ-pedsql.sas

Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score (responders ≥ 15)

Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Week 24	n (%)	20 (100.00)	9 (100.00)
	Self-report: n (%)	9 (45.00)	4 (44.44)
	Parent Report: n (%)	9 (45.00)	4 (44.44)
	Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
	Number of patients imputed as non-responders: n (%)	2 (10.00)	1 (11.11)
	Non-Responders [1]	16 (80.00)	8 (88.89)
	Responders	4 (20.00)	1 (11.11)
	OR (95% CI)	2.00 (0.19, 20.97)	
	RR (95% CI)	1.80 (0.23, 13.92)	
	RD % (95% CI)	8.89 (-18.11, 35.89)	
	p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Data Pooled Across all Age groups
Table Generation: 11SEP2023 12:10:18 PM
Program: t-qs-categ-pedsql.sas

4.6.2 Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score (responders ≥ 15)

Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Week 12	n (%)	20 (100.00)	9 (100.00)
	Self-report: n (%)	10 (50.00)	4 (44.44)
	Parent Report: n (%)	9 (45.00)	3 (33.33)
	Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
	Number of patients imputed as non-responders: n (%)	1 (5.00)	2 (22.22)
	Non-Responders [1]	16 (80.00)	8 (88.89)
	Responders	4 (20.00)	1 (11.11)
	OR (95% CI)	2.00 (0.19, 20.97)	
	RR (95% CI)	1.80 (0.23, 13.92)	
	RD % (95% CI)	8.89 (-18.11, 35.89)	
	p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Data Pooled Across all Age groups
Table Generation: 11SEP2023 12:10:24 PM
Program: t-qs-categ-pedsql.sas

Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score (responders ≥ 15)

Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Week 24	n (%)	20 (100.00)	9 (100.00)
	Self-report: n (%)	9 (45.00)	4 (44.44)
	Parent Report: n (%)	8 (40.00)	4 (44.44)
	Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
	Number of patients imputed as non-responders: n (%)	3 (15.00)	1 (11.11)
	Non-Responders [1]	14 (70.00)	8 (88.89)
	Responders	6 (30.00)	1 (11.11)
	OR (95% CI)	3.43 (0.35, 33.80)	
	RR (95% CI)	2.70 (0.38, 19.27)	
	RD % (95% CI)	18.89 (-9.83, 47.61)	
	p-value – Fisher's Exact Test	0.3816	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Data Pooled Across all Age groups
Table Generation: 11SEP2023 12:10:24 PM
Program: t-qs-categ-pedsql.sas

4.6.3 Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score (responders ≥ 15)

Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Week 12	n (%)	20 (100.00)	9 (100.00)
	Self-report: n (%)	10 (50.00)	4 (44.44)
	Parent Report: n (%)	9 (45.00)	3 (33.33)
	Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
	Number of patients imputed as non-responders: n (%)	1 (5.00)	2 (22.22)
	Non-Responders [1]	18 (90.00)	9 (100.00)
	Responders	2 (10.00)	0 (0.00)
	OR (95% CI)	2.57 (0.11, 59.06)	
	RR (95% CI)	2.38 (0.13, 45.11)	
	RD % (95% CI)	6.90 (-12.44, 26.25)	
	p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Data Pooled Across all Age groups
Table Generation: 11SEP2023 12:10:30 PM
Program: t-qs-categ-pedsql.sas

Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score (responders ≥ 15)

Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Week 24	n (%)	20 (100.00)	9 (100.00)
	Self-report: n (%)	9 (45.00)	4 (44.44)
	Parent Report: n (%)	8 (40.00)	4 (44.44)
	Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
	Number of patients imputed as non-responders: n (%)	3 (15.00)	1 (11.11)
	Non-Responders [1]	17 (85.00)	8 (88.89)
	Responders	3 (15.00)	1 (11.11)
	OR (95% CI)	1.41 (0.13, 15.78)	
	RR (95% CI)	1.35 (0.16, 11.27)	
	RD % (95% CI)	3.89 (-21.93, 29.70)	
	p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Data Pooled Across all Age groups
Table Generation: 11SEP2023 12:10:30 PM
Program: t-qs-categ-pedsql.sas

4.7 Tipping-Point-Analysen für signifikante Endpunkte

4.7.1 Plasma arginine level

Note:
Tipping point analysis not done due to no missing data at 24 weeks.

Program: t-pd-tipping.sas
Table Generation: 11SEP2023 9:12:57 AM

4.7.2 Argininic acid levels

Note:
Tipping point analysis not done due to no missing data at 24 weeks.

Program: t-pd-tipping.sas
Table Generation: 11SEP2023 9:12:59 AM

4.7.3 Guanidinoacetic acid levels

Note:
Tipping point analysis not done due to no missing data at 24 weeks.

Program: t-pd-tipping.sas
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4.7.4 Alpha-keto-δ-guanidinovaleric acid levels

Note:
Tipping point analysis not done due to no missing data at 24 weeks.

Program: t-pd-tipping.sas
Table Generation: 11SEP2023 9:13:02 AM

4.7.5 Alpha-N-acetylarginine levels

Note:
Tipping point analysis not done due to no missing data at 24 weeks.

Program: t-pd-tipping.sas
Table Generation: 11SEP2023 9:13:04 AM

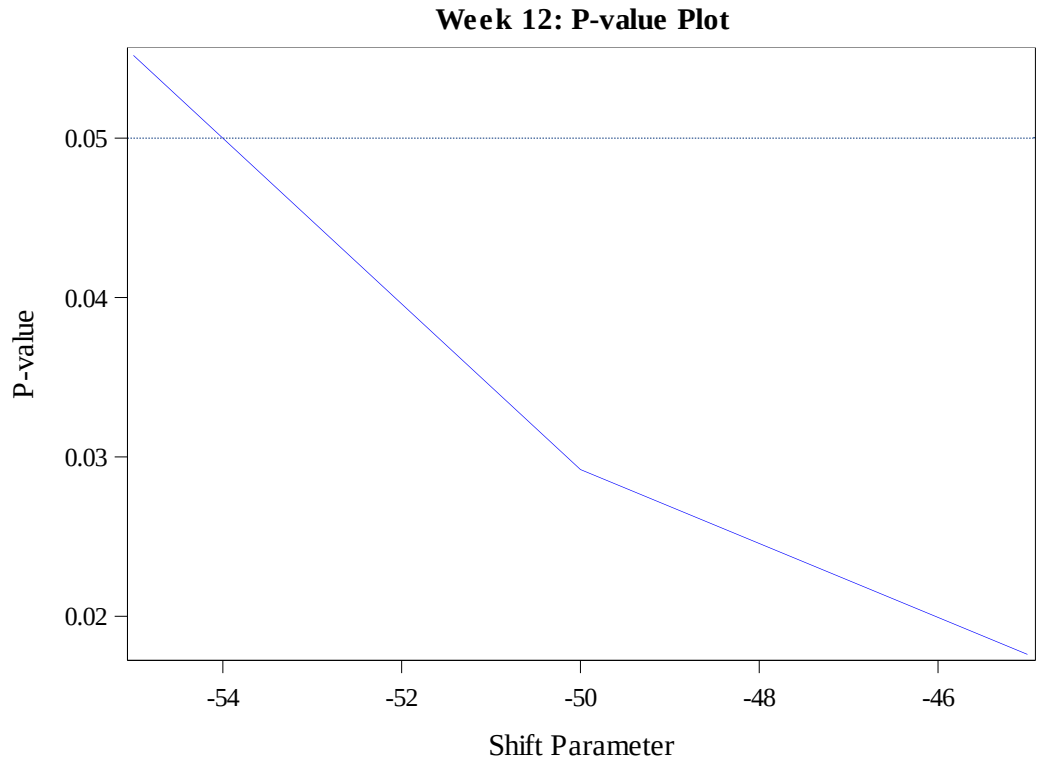
4.7.6 Ornithine levels

Week 12: Finding Tipping Point for Ornithine (uM)

Shift	Treatment	GLS Mean (log-scale SE)	GLS Mean CI	Difference	Difference CI	p-value MMRM[1]
Original	Pegzilarginase	2.14 (0.088)	1.79, 2.57	2.27	1.69, 3.05	<0.0001
	Placebo	0.94 (0.108)	0.75, 1.18			
-45	Pegzilarginase	1.68 (0.170)	1.20, 2.34	1.86	1.11, 3.10	0.0176
	Placebo	0.90 (0.206)	0.60, 1.35			
-50	Pegzilarginase	1.64 (0.178)	1.16, 2.33	1.81	1.06, 3.09	0.0292
	Placebo	0.91 (0.209)	0.60, 1.37			
-55	Pegzilarginase	1.59 (0.199)	1.08, 2.35	1.76	0.99, 3.13	0.0552
	Placebo	0.91 (0.223)	0.59, 1.40			

Abbreviations: SE = Standard error; LS = Least Squares; GLS = Geometric Least Squares; MMRM = Mixed Model Repeated Measures; CI = confidence interval.
[1] Based on a MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
The tipping point analyses were performed using SAS PROC MI with a MNAR statement and the ADJUST option in order to shift the distribution towards a less favorable outcome for missing data in the Pegzilarginase group.
Program: t-pd-tipping.sas
Table Generation: 11SEP2023 9:13:42 AM

Ornithine levels



Abbreviations: SE = Standard error; LS = Least Squares; GLS = Geometric Least Squares; MMRM = Mixed Model Repeated Measures; CI = confidence interval.
[1] Based on a MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

The tipping point analyses were performed using SAS PROC MI with a MNAR statement and the ADJUST option in order to shift the distribution towards a less favorable outcome for missing data in the Pegzilarginase group.

Program: t-pd-tipping.sas

Table Generation: 11SEP2023 9:13:42 AM

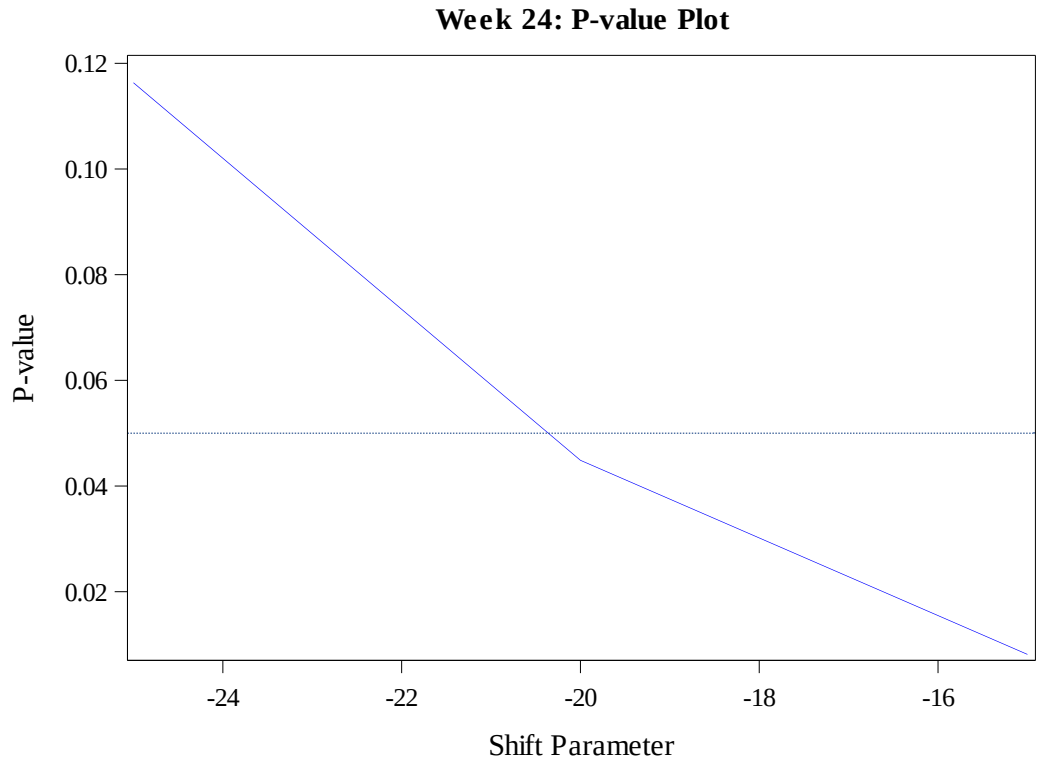
Ornithine levels

Week 24: Finding Tipping Point for Ornithine (uM)

Shift	Treatment	GLS Mean (log-scale SE)	GLS Mean CI	Difference	Difference CI	p-value MMRM[1]
Original	Pegzilarginase	1.94 (0.083)	1.63, 2.31	2.07	1.57, 2.73	<0.0001
	Placebo	0.94 (0.102)	0.76, 1.16			
-15	Pegzilarginase	1.64 (0.166)	1.18, 2.27	1.83	1.17, 2.86	0.0081
	Placebo	0.90 (0.177)	0.63, 1.27			
-20	Pegzilarginase	1.52 (0.194)	1.04, 2.23	1.70	1.01, 2.86	0.0449
	Placebo	0.90 (0.200)	0.60, 1.33			
-25	Pegzilarginase	1.42 (0.215)	0.93, 2.16	1.59	0.89, 2.82	0.1163
	Placebo	0.89 (0.225)	0.58, 1.39			

Abbreviations: SE = Standard error; LS = Least Squares; GLS = Geometric Least Squares; MMRM = Mixed Model Repeated Measures; CI = confidence interval.
[1] Based on a MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
The tipping point analyses were performed using SAS PROC MI with a MNAR statement and the ADJUST option in order to shift the distribution towards a less favorable outcome for missing data in the Pegzilarginase group.
Program: t-pd-tipping.sas
Table Generation: 11SEP2023 9:13:42 AM

Ornithine levels



Abbreviations: SE = Standard error; LS = Least Squares; GLS = Geometric Least Squares; MMRM = Mixed Model Repeated Measures; CI = confidence interval.
[1] Based on a MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
The tipping point analyses were performed using SAS PROC MI with a MNAR statement and the ADJUST option in order to shift the distribution towards a less favorable outcome for missing data in the Pegzilarginase group.

Program: t-pd-tipping.sas
Table Generation: 11SEP2023 9:13:42 AM

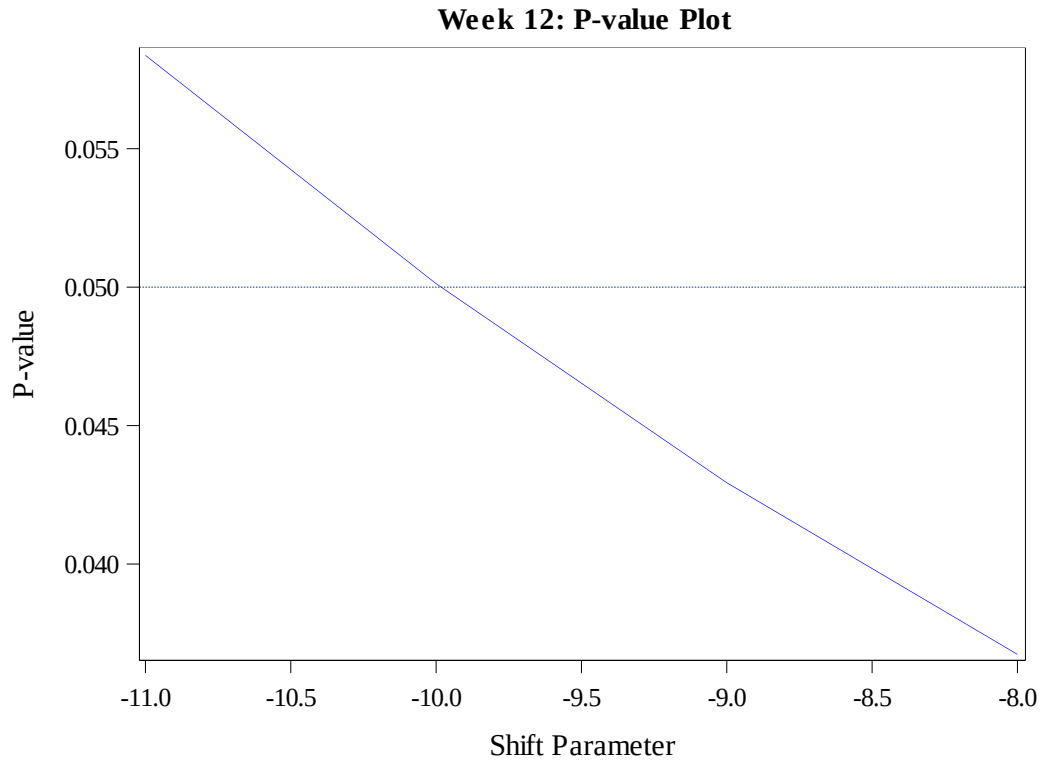
4.7.7 GMFM-D

Week 12: Finding Tipping Point for GMFM-D

Shift	Treatment	LS Mean (SE)	LS Mean CI	Difference	Difference CI	p-value MMRM[1]
Original	Pegzilarginase	2.74 (0.835)	1.03, 4.46	3.43	0.55, 6.32	0.0216
	Placebo	-0.69 (1.125)	-3.00, 1.63			
-8	Pegzilarginase	2.41 (0.885)	0.67, 4.14	3.14	0.19, 6.08	0.0367
	Placebo	-0.73 (1.204)	-3.09, 1.63			
-9	Pegzilarginase	2.36 (0.900)	0.60, 4.13	3.09	0.10, 6.08	0.0429
	Placebo	-0.73 (1.224)	-3.13, 1.67			
-10	Pegzilarginase	2.32 (0.916)	0.52, 4.11	3.05	-0.00, 6.09	0.0501
	Placebo	-0.73 (1.247)	-3.17, 1.72			
-11	Pegzilarginase	2.27 (0.934)	0.44, 4.10	3.00	-0.11, 6.11	0.0584
	Placebo	-0.73 (1.272)	-3.22, 1.76			

Abbreviations: SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = confidence interval.
[1] Based on a MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
The tipping point analyses were performed using SAS PROC MI with a MNAR statement and the ADJUST option in order to shift the distribution towards a less favorable outcome for missing data in the Pegzilarginase group.
Program: t-qs-tipping.sas
Table Generation: 11SEP2023 2:22:54 PM

GMFM-D



Abbreviations: SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = confidence interval.
[1] Based on a MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
The tipping point analyses were performed using SAS PROC MI with a MNAR statement and the ADJUST option in order to shift the distribution towards a less favorable outcome for missing data in the Pegzilarginase group.

Program: t-qs-tipping.sas
Table Generation: 11SEP2023 2:22:54 PM

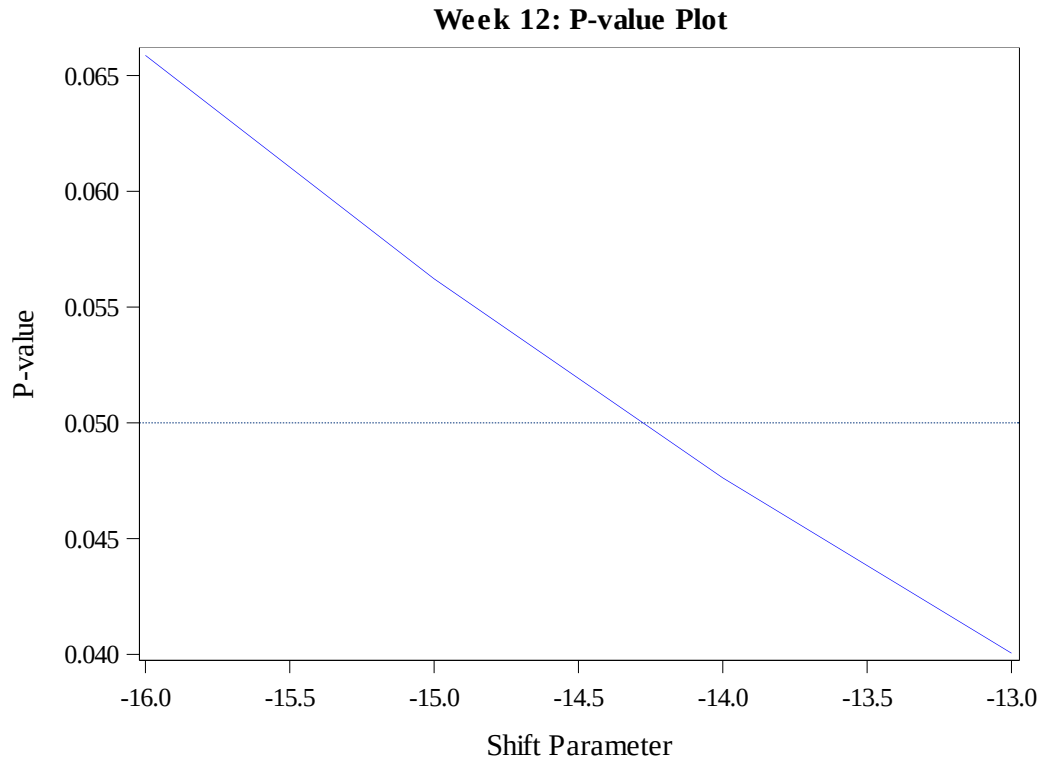
4.7.8 GMFM-D - excluding subject with data entry error

Week 12: Finding Tipping Point for GMFM-D - excluding subject with data entry error

Shift	Treatment	LS Mean (SE)	LS Mean CI	Difference	Difference CI	p-value MMRM[1]
Original	Pegzilarginase	2.68 (0.795)	1.04, 4.32	4.11	1.27, 6.95	0.0065
	Placebo	-1.43 (1.124)	-3.75, 0.89			
-13	Pegzilarginase	2.07 (0.958)	0.19, 3.95	3.44	0.16, 6.72	0.0401
	Placebo	-1.37 (1.350)	-4.02, 1.28			
-14	Pegzilarginase	2.02 (0.980)	0.10, 3.94	3.39	0.04, 6.74	0.0476
	Placebo	-1.37 (1.379)	-4.07, 1.34			
-15	Pegzilarginase	1.97 (1.002)	0.01, 3.94	3.34	-0.09, 6.77	0.0562
	Placebo	-1.37 (1.410)	-4.13, 1.40			
-16	Pegzilarginase	1.93 (1.026)	-0.09, 3.94	3.29	-0.22, 6.79	0.0659
	Placebo	-1.36 (1.442)	-4.19, 1.46			

Abbreviations: SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = confidence interval.
[1] Based on a MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
The tipping point analyses were performed using SAS PROC MI with a MNAR statement and the ADJUST option in order to shift the distribution towards a less favorable outcome for missing data in the Pegzilarginase group.
Program: t-qs-tipping.sas
Table Generation: 11SEP2023 2:23:10 PM

GMFM-D - excluding subject with data entry error



Abbreviations: SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = confidence interval.
[1] Based on a MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
The tipping point analyses were performed using SAS PROC MI with a MNAR statement and the ADJUST option in order to shift the distribution towards a less favorable outcome for missing data in the Pegzilarginase group.

Program: t-qs-tipping.sas
Table Generation: 11SEP2023 2:23:10 PM

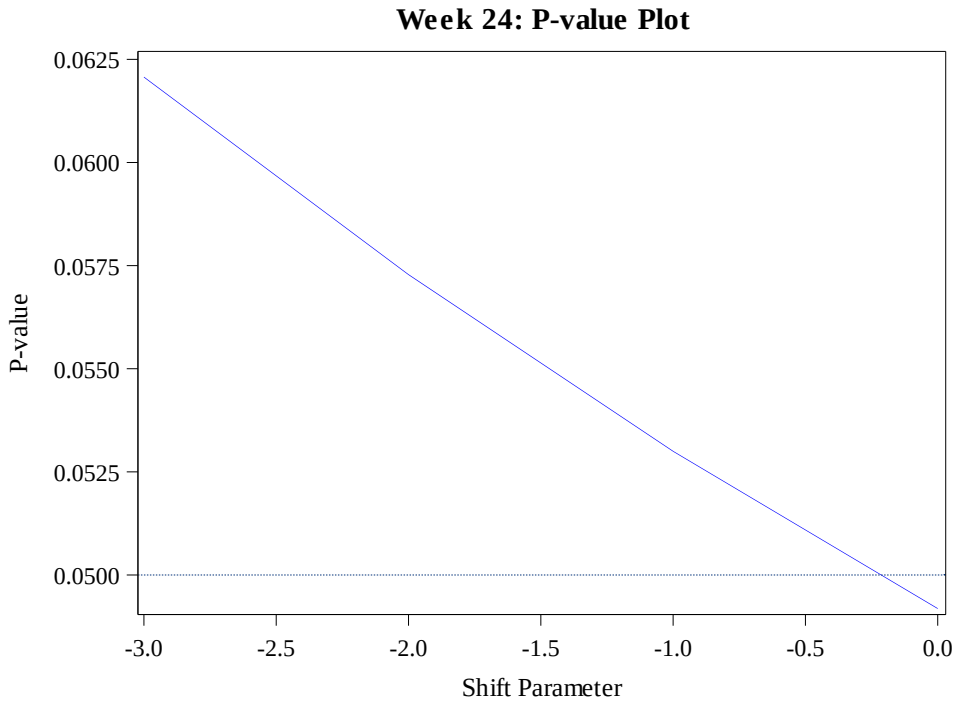
4.7.9 Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score

Week 24: Finding Tipping Point for PedsQL Total Scale Score

Shift	Treatment	LS Mean (SE)	LS Mean CI	Difference	Difference CI	p-value MMRM[1]
Original	Pegzilarginase	0.99 (2.598)	-4.37, 6.35	10.25	0.49, 20.01	0.0402
	Placebo	-9.26 (3.908)	-17.31, -1.21			
0	Pegzilarginase	1.86 (2.582)	-3.20, 6.92	9.23	0.03, 18.43	0.0492
	Placebo	-7.37 (3.844)	-14.90, 0.17			
-1	Pegzilarginase	1.73 (2.588)	-3.34, 6.81	9.10	-0.12, 18.32	0.0530
	Placebo	-7.37 (3.854)	-14.92, 0.19			
-2	Pegzilarginase	1.60 (2.596)	-3.48, 6.69	8.97	-0.28, 18.22	0.0573
	Placebo	-7.37 (3.868)	-14.95, 0.21			
-3	Pegzilarginase	1.47 (2.607)	-3.64, 6.58	8.84	-0.45, 18.13	0.0621
	Placebo	-7.37 (3.886)	-14.98, 0.25			

Abbreviations: SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = confidence interval.
[1] Based on a MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
The tipping point analyses were performed using SAS PROC MI with a MNAR statement and the ADJUST option in order to shift the distribution towards a less favorable outcome for missing data in the Pegzilarginase group.
NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Program: t-qs-tipping.sas
Table Generation: 11SEP2023 2:23:39 PM

Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score



Abbreviations: SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = confidence interval.
[1] Based on a MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
The tipping point analyses were performed using SAS PROC MI with a MNAR statement and the ADJUST option in order to shift the distribution towards a less favorable outcome for missing data in the Pegzilarginase group.
NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.

Program: t-qs-tipping.sas
Table Generation: 11SEP2023 2:23:39 PM

4.7.10 CaGI-S ability to walk

Note:
Tipping point analysis was not reasonable because the p-value becomes greater than 0.05 regardless of how small shift is.

Abbreviations: SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = confidence interval.
[1] Based on a MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
The tipping point analyses were performed using SAS PROC MI with a MNAR statement and the ADJUST option in order to shift the distribution towards a less favorable outcome for missing data in the Pegzilarginase group.
Program: t-qs-tipping.sas
Table Generation: 11SEP2023 2:24:11 PM

4.8 Wilcoxon-Rangsummen-Test für die Endpunkte 2MWT, GMFM, FMS, GFAQ, VABS-II und klinisch relevante Laborparameter

Endpunkt	p-Wert Wilcoxon Rangsummentest
Krankheitsspezifische Laborparameter	
Arginin-Konzentration im Plasma	**< 0,0001**
GC-Konzentration im Plasma	
ArgA	**< 0,0001**
GAA	**< 0,0001**
GVA	**< 0,0001**
NAA	**< 0,0001**
Ornithin-Konzentration im Plasma	**0,0192**
2MWT	0,3790
GMFM	
Hauptanalysen	
GMFM-D	0,0529
GMFM-E	0,3207
Sensitivitätsanalysen[a]	
GMFM-D	0,0939
GMFM-E	0,1544
FMS	
FMS-5	0,8660
FMS-50	1,0000
FMS-500	0,5394
GFAQ	0,2647

Endpunkt	p-Wert Wilcoxon Rangsummentest
VABS-II	
Hauptanalysen	
Kommunikation	1,0000
Alltagskompetenz	0,6764
Sozialisierung	0,3544
Motorische Fähigkeiten	0,3333
ABCS	1,0000
Sensitivitätsanalyse[b]	
ABCS	0,9577
Sensitivitätsanalyse[c]	
Motorische Fähigkeiten	0,1429

ABCS: *Adaptive Behaviour Composite Score*, ArgA: *Argininic Acid*, FMS: *Functional Mobility Scale*, GAA: *Guanidinoacetic Acid*, GC: *Guanidino Compund*, GFAQ: *Gillette Functional Assessment Questionnaire*, *GMFM: Gross Motor Function Measure-88*, GVA: *Alpha-Keto-Delta-Guanidinovaleric Acid*, NAA: *N-Acetyl-L-Arginin*, VABS-II: *Vineland Adaptive Behavior Scales, Second Edition*,

a) Für einen Patienten wurde kein Baseline-Wert für den GMFM-D erhoben, jedoch als Wert irrtümlicherweise „0“ eingetragen und beim GMFM-E ein unvollständig ausgefüllter Fragebogen zu Baseline wie ein vollständig ausgefüllter Fragebogen ausgewertet. Diese „0“ bzw. der unvollständig ausgefüllte Fragebogen wurde für die Sensitivitätsanalyse dementsprechend zu einem fehlenden Wert korrigiert.

b) Unter Berücksichtigung von 2 Patienten, die bei der initialen Analyse des CSR irrtümlich für die Auswertung des ABCS nicht berücksichtigt wurden

c) In die Hauptanalyse gingen auch die Ergebnisse eines Patienten ein, dessen Messwerte durch Datenerhebungsfehler außerhalb der Skalenspannweite lagen, was nach Database Lock bemerkt wurde. Diese Daten wurden in der Sensitivitätsanalyse als fehlende Werte ersetzt.

4.9 Analysen zu Verträglichkeitsendpunkten

4.9.1 Verträglichkeitsendpunkten (Gesamtraten inklusive krankheitsbezogener Ereignisse)

4.9.1.1 Patients with at least one TEAE

Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Patients with any TEAEs	18 (85.71)	11 (100.00)
Patients with no TEAEs	3 (14.29)	0 (0.00)
OR (95% CI)	0.23 (0.01, 4.87)	
RR (95% CI)	0.88 (0.71, 1.09)	
RD % (95% CI)	-11.74 (-30.75, 7.27)	
p-value – Fisher's Exact Test	0.5343	

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-teae.sas
Table Generation: 11SEP2023 2:28:42 PM

4.9.1.2 Patients with at least one mild TEAE

Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Patients with any mild TEAEs	17 (80.95)	10 (90.91)
Patients with no mild TEAEs	4 (19.05)	1 (9.09)
OR (95% CI)	0.43 (0.04, 4.35)	
RR (95% CI)	0.89 (0.67, 1.18)	
RD % (95% CI)	-9.96 (-33.85, 13.93)	
p-value – Fisher's Exact Test	0.6367	

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-teae.sas
Table Generation: 11SEP2023 2:28:53 PM

4.9.1.3 Patients with at least one moderate TEAE

Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Patients with any moderate TEAEs	8 (38.10)	6 (54.55)
Patients with no moderate TEAEs	13 (61.90)	5 (45.45)
OR (95% CI)	0.51 (0.12, 2.25)	
RR (95% CI)	0.70 (0.32, 1.50)	
RD % (95% CI)	-16.45 (-52.47, 19.57)	
p-value – Fisher's Exact Test	0.4651	

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-teae.sas
Table Generation: 11SEP2023 2:29:00 PM

4.9.1.4 Patients with at least one severe TEAE

Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Patients with any severe TEAEs	1 (4.76)	0 (0.00)
Patients with no severe TEAEs	20 (95.24)	11 (100.00)
OR (95% CI)	1.68 (0.06, 44.77)	
RR (95% CI)	1.64 (0.07, 37.15)	
RD % (95% CI)	2.65 (-12.80, 18.10)	
p-value – Fisher's Exact Test	1.0000	

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-teae.sas
Table Generation: 11SEP2023 2:29:07 PM

4.9.1.5 Hypersensitivity reactions by severity (non-severe, severe, serious)

Severity	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-Severe	Patients with any hypersensitivity reactions	2 (9.52)	0 (0.00)
	Patients with no hypersensitivity reactions	19 (90.48)	11 (100.00)
	OR (95% CI)	2.95 (0.13, 66.95)	
	RR (95% CI)	2.73 (0.14, 52.30)	
	RD % (95% CI)	7.20 (-10.23, 24.62)	
	p-value – Fisher's Exact Test	0.5343	
Severe	Patients with any hypersensitivity reactions	0 (0.00)	0 (0.00)
	Patients with no hypersensitivity reactions	21 (100.00)	11 (100.00)
Serious	Patients with any hypersensitivity reactions	0 (0.00)	0 (0.00)
	Patients with no hypersensitivity reactions	21 (100.00)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Hypersensitivity reactions include the MedDRA PT of Hypersensitivity, and/or events that the investigator identified as Hypersensitivity TEAESI.
Non-Severe = Mild and moderate TEAEs; Severe = Severe TEAEs; Serious = Any TEAE flagged as serious.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-teae-sev.sas
Table Generation: 11SEP2023 2:31:57 PM

4.9.1.6 Injection site reactions by severity (non-severe, severe, serious)

Severity	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-Severe	Patients with any injection site reactions	0 (0.00)	0 (0.00)
	Patients with no injection site reactions	21 (100.00)	11 (100.00)
Severe	Patients with any injection site reactions	0 (0.00)	0 (0.00)
	Patients with no injection site reactions	21 (100.00)	11 (100.00)
Serious	Patients with any injection site reactions	0 (0.00)	0 (0.00)
	Patients with no injection site reactions	21 (100.00)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
For Injection site reactions, the MedDRA High Level Term Injection Site Reactions is included.
Non-Severe = Mild and moderate TEAEs; Severe = Severe TEAEs; Serious = Any TEAE flagged as serious.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-teae-sev.sas
Table Generation: 11SEP2023 2:32:04 PM

4.9.1.7 Hyperammonemic episodes by severity (non-severe, severe, serious)

Severity	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-Severe	Patients with any hyperammonemic episodes	3 (14.29)	4 (36.36)
	Patients with no hyperammonemic episodes	18 (85.71)	7 (63.64)
	OR (95% CI)	0.29 (0.05, 1.65)	
	RR (95% CI)	0.39 (0.11, 1.45)	
	RD % (95% CI)	-22.08 (-54.20, 10.05)	
	p-value – Fisher's Exact Test	0.1967	
Severe	Patients with any hyperammonemic episodes	1 (4.76)	0 (0.00)
	Patients with no hyperammonemic episodes	20 (95.24)	11 (100.00)
	OR (95% CI)	1.68 (0.06, 44.77)	
	RR (95% CI)	1.64 (0.07, 37.15)	
	RD % (95% CI)	2.65 (-12.80, 18.10)	
	p-value – Fisher's Exact Test	1.0000	
Serious	Patients with any hyperammonemic episodes	3 (14.29)	4 (36.36)
	Patients with no hyperammonemic episodes	18 (85.71)	7 (63.64)
	OR (95% CI)	0.29 (0.05, 1.65)	
	RR (95% CI)	0.39 (0.11, 1.45)	
	RD % (95% CI)	-22.08 (-54.20, 10.05)	
	p-value – Fisher's Exact Test	0.1967	

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
For Hyperammonemic episodes, the following MedDRA Preferred Terms are included: Hyperammonaemia, Hyperammonaemic crisis, Hyperammonaemic encephalopathy.
Non-Severe = Mild and moderate TEAEs; Severe = Severe TEAEs; Serious = Any TEAE flagged as serious.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.9.1.8 Liver function test TEAE by severity (non-severe, severe, serious)

Severity	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-Severe	Patients with any liver function test TEAEs	4 (19.05)	2 (18.18)
	Patients with no liver function test TEAEs	17 (80.95)	9 (81.82)
	OR (95% CI)	1.06 (0.16, 6.94)	
	RR (95% CI)	1.05 (0.23, 4.85)	
	RD % (95% CI)	0.87 (-27.45, 29.18)	
	p-value – Fisher's Exact Test	1.0000	
Severe	Patients with any liver function test TEAEs	1 (4.76)	0 (0.00)
	Patients with no liver function test TEAEs	20 (95.24)	11 (100.00)
	OR (95% CI)	1.68 (0.06, 44.77)	
	RR (95% CI)	1.64 (0.07, 37.15)	
	RD % (95% CI)	2.65 (-12.80, 18.10)	
	p-value – Fisher's Exact Test	1.0000	
Serious	Patients with any liver function test TEAEs	0 (0.00)	0 (0.00)
	Patients with no liver function test TEAEs	21 (100.00)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
For Liver Function Test TEAEs, the MedDRA High Level Term (HLT) 'Liver function analyses' is included.
Non-Severe = Mild and moderate TEAEs; Severe = Severe TEAEs; Serious = Any TEAE flagged as serious.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.9.1.9 Any TEAEs by SOC and PT

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Blood and lymphatic system disorders	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
		Patients with no TEAEs	19 (90.48)	11 (100.00)
	Anaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Iron deficiency anaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
Eye disorders	Total	Patients with any TEAEs	4 (19.05)	0 (0.00)
		Patients with no TEAEs	17 (80.95)	11 (100.00)
		OR (95% CI)	5.91 (0.29, 120.58)	
		RR (95% CI)	4.91 (0.29, 83.67)	
		RD % (95% CI)	16.29 (-4.01, 36.58)	
		p-value – Fisher's Exact Test	0.2720	
	Eye irritation	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Eye pain	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-teae-soc.sas
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Any TEAEs by SOC and PT

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Eye disorders	Eyelid oedema	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Ocular hyperaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
Gastrointestinal disorders	Total	Patients with any TEAEs	10 (47.62)	6 (54.55)
		Patients with no TEAEs	11 (52.38)	5 (45.45)
		OR (95% CI)	0.76 (0.18, 3.27)	
		RR (95% CI)	0.87 (0.43, 1.76)	
		RD % (95% CI)	-6.93 (-43.29, 29.43)	
		p-value – Fisher's Exact Test	1.0000	
	Abdominal discomfort	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-teae-soc.sas
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Any TEAEs by SOC and PT

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Gastrointestinal disorders	Abdominal pain	Patients with any TEAEs	1 (4.76)	3 (27.27)
		Patients with no TEAEs	20 (95.24)	8 (72.73)
		OR (95% CI)	0.13 (0.01, 1.48)	
		RR (95% CI)	0.17 (0.02, 1.49)	
		RD % (95% CI)	-22.51 (-50.36, 5.34)	
		p-value – Fisher's Exact Test	0.1055	
	Abdominal pain upper	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Anal rash	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Constipation	Patients with any TEAEs	3 (14.29)	1 (9.09)
		Patients with no TEAEs	18 (85.71)	10 (90.91)
		OR (95% CI)	1.67 (0.15, 18.22)	
		RR (95% CI)	1.57 (0.18, 13.39)	
		RD % (95% CI)	5.19 (-17.45, 27.84)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-teae-soc.sas
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Any TEAEs by SOC and PT

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Gastrointestinal disorders	Diarrhoea	Patients with any TEAEs	1 (4.76)	1 (9.09)
		Patients with no TEAEs	20 (95.24)	10 (90.91)
	Haematochezia	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Nausea	Patients with any TEAEs	1 (4.76)	4 (36.36)
		Patients with no TEAEs	20 (95.24)	7 (63.64)
		OR (95% CI)	0.09 (0.01, 0.92)	
		RR (95% CI)	0.13 (0.02, 1.03)	
		RD % (95% CI)	-31.60 (-61.45, -1.75)	
		p-value – Fisher's Exact Test	0.0367 ***	
	Oral pain	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Any TEAEs by SOC and PT

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Gastrointestinal disorders	Vomiting	Patients with any TEAEs	6 (28.57)	3 (27.27)
		Patients with no TEAEs	15 (71.43)	8 (72.73)
		OR (95% CI)	1.07 (0.21, 5.44)	
		RR (95% CI)	1.05 (0.32, 3.40)	
		RD % (95% CI)	1.30 (-31.35, 33.95)	
		p-value – Fisher's Exact Test	1.0000	
General disorders and administration site conditions	Total	Patients with any TEAEs	7 (33.33)	0 (0.00)
		Patients with no TEAEs	14 (66.67)	11 (100.00)
		OR (95% CI)	11.90 (0.61, 230.84)	
		RR (95% CI)	8.18 (0.51, 131.22)	
		RD % (95% CI)	29.92 (7.12, 52.73)	
		p-value – Fisher's Exact Test	0.0664	
	Administration site extravasation	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Asthenia	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Any TEAEs by SOC and PT

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
General disorders and administration site conditions	Illness	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Infusion site extravasation	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Oedema peripheral	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Peripheral swelling	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Pyrexia	Patients with any TEAEs	4 (19.05)	0 (0.00)
		Patients with no TEAEs	17 (80.95)	11 (100.00)
		OR (95% CI)	5.91 (0.29, 120.58)	
		RR (95% CI)	4.91 (0.29, 83.67)	
		RD % (95% CI)	16.29 (-4.01, 36.58)	
		p-value – Fisher's Exact Test	0.2720	
	Swelling face	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Any TEAEs by SOC and PT

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Hepatobiliary disorders	Total	Patients with any TEAEs	2 (9.52)	1 (9.09)
		Patients with no TEAEs	19 (90.48)	10 (90.91)
	Cholelithiasis	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Hepatic cytolysis	Patients with any TEAEs	1 (4.76)	1 (9.09)
		Patients with no TEAEs	20 (95.24)	10 (90.91)
Immune system disorders	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
		Patients with no TEAEs	19 (90.48)	11 (100.00)
	Food allergy	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Hypersensitivity	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Any TEAEs by SOC and PT

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Infections and infestations	Total	Patients with any TEAEs	8 (38.10)	0 (0.00)
		Patients with no TEAEs	13 (61.90)	11 (100.00)
		OR (95% CI)	14.48 (0.75, 279.08)	
		RR (95% CI)	9.27 (0.58, 147.11)	
		RD % (95% CI)	34.47 (11.19, 57.75)	
		p-value – Fisher's Exact Test	0.0292 ***	
	Conjunctivitis	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Fungal skin infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Gastrointestinal viral infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Influenza	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Nasopharyngitis	Patients with any TEAEs	2 (9.52)	0 (0.00)
		Patients with no TEAEs	19 (90.48)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Any TEAEs by SOC and PT

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Infections and infestations	Pharyngitis	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Respiratory syncytial virus infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Upper respiratory tract infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Viral infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
Injury, poisoning and procedural complications	Total	Patients with any TEAEs	5 (23.81)	0 (0.00)
		Patients with no TEAEs	16 (76.19)	11 (100.00)
		OR (95% CI)	7.67 (0.39, 152.66)	
		RR (95% CI)	6.00 (0.36, 99.49)	
		RD % (95% CI)	20.83 (-0.50, 42.17)	
		p-value – Fisher's Exact Test	0.1378	
	Contusion	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-teae-soc.sas
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Any TEAEs by SOC and PT

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Injury, poisoning and procedural complications	Eye injury	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Fall	Patients with any TEAEs	2 (9.52)	0 (0.00)
		Patients with no TEAEs	19 (90.48)	11 (100.00)
	Procedural pain	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Scratch	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
Investigations	Total	Patients with any TEAEs	7 (33.33)	3 (27.27)
		Patients with no TEAEs	14 (66.67)	8 (72.73)
		OR (95% CI)	1.33 (0.27, 6.65)	
		RR (95% CI)	1.22 (0.39, 3.82)	
		RD % (95% CI)	6.06 (-27.09, 39.21)	
		p-value – Fisher's Exact Test	1.0000	
	Activated partial thromboplastin time prolonged	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Any TEAEs by SOC and PT

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Investigations	Alanine aminotransferase increased	Patients with any TEAEs	2 (9.52)	0 (0.00)
		Patients with no TEAEs	19 (90.48)	11 (100.00)
	Amino acid level increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Ammonia increased	Patients with any TEAEs	3 (14.29)	2 (18.18)
		Patients with no TEAEs	18 (85.71)	9 (81.82)
		OR (95% CI)	0.75 (0.11, 5.32)	
		RR (95% CI)	0.79 (0.15, 4.03)	
		RD % (95% CI)	-3.90 (-31.16, 23.37)	
		p-value – Fisher's Exact Test	1.0000	
	Aspartate aminotransferase increased	Patients with any TEAEs	2 (9.52)	0 (0.00)
		Patients with no TEAEs	19 (90.48)	11 (100.00)
	Blood alkaline phosphatase increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Blood potassium decreased	Patients with any TEAEs	0 (0.00)	1 (9.09)
		Patients with no TEAEs	21 (100.00)	10 (90.91)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Any TEAEs by SOC and PT

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Investigations	Blood pressure increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Body temperature increased	Patients with any TEAEs	0 (0.00)	1 (9.09)
		Patients with no TEAEs	21 (100.00)	10 (90.91)
	Cardiac murmur	Patients with any TEAEs	1 (4.76)	1 (9.09)
		Patients with no TEAEs	20 (95.24)	10 (90.91)
	Electroencephalogram abnormal	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	International normalised ratio increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Prothrombin time prolonged	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Any TEAEs by SOC and PT

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Metabolism and nutrition disorders	Total	Patients with any TEAEs	3 (14.29)	4 (36.36)
		Patients with no TEAEs	18 (85.71)	7 (63.64)
		OR (95% CI)	0.29 (0.05, 1.65)	
		RR (95% CI)	0.39 (0.11, 1.45)	
		RD % (95% CI)	-22.08 (-54.20, 10.05)	
		p-value – Fisher's Exact Test	0.1967	
	Decreased appetite	Patients with any TEAEs	0 (0.00)	2 (18.18)
		Patients with no TEAEs	21 (100.00)	9 (81.82)
		OR (95% CI)	0.09 (0.00, 2.02)	
		RR (95% CI)	0.11 (0.01, 2.09)	
		RD % (95% CI)	-18.56 (-42.37, 5.25)	
		p-value – Fisher's Exact Test	0.1109	

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Any TEAEs by SOC and PT

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Metabolism and nutrition disorders	Hyperammonaemia	Patients with any TEAEs	2 (9.52)	3 (27.27)
		Patients with no TEAEs	19 (90.48)	8 (72.73)
		OR (95% CI)	0.28 (0.04, 2.01)	
		RR (95% CI)	0.35 (0.07, 1.79)	
		RD % (95% CI)	-17.75 (-46.91, 11.41)	
		p-value – Fisher's Exact Test	0.3098	
	Hypokalaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Vitamin D deficiency	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Vitamin K deficiency	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Zinc deficiency	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-teae-soc.sas
Table Generation: 11SEP2023 2:37:10 PM

Any TEAEs by SOC and PT

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Musculoskeletal and connective tissue disorders	Total	Patients with any TEAEs	1 (4.76)	2 (18.18)
		Patients with no TEAEs	20 (95.24)	9 (81.82)
		OR (95% CI)	0.23 (0.02, 2.81)	
		RR (95% CI)	0.26 (0.03, 2.58)	
		RD % (95% CI)	-13.42 (-37.97, 11.13)	
		p-value – Fisher's Exact Test	0.2661	
	Arthralgia	Patients with any TEAEs	0 (0.00)	1 (9.09)
		Patients with no TEAEs	21 (100.00)	10 (90.91)
	Muscle spasms	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Osteochondrosis	Patients with any TEAEs	0 (0.00)	1 (9.09)
		Patients with no TEAEs	21 (100.00)	10 (90.91)
	Pain in extremity	Patients with any TEAEs	0 (0.00)	1 (9.09)
		Patients with no TEAEs	21 (100.00)	10 (90.91)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-teae-soc.sas
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Any TEAEs by SOC and PT

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Nervous system disorders	Total	Patients with any TEAEs	5 (23.81)	3 (27.27)
		Patients with no TEAEs	16 (76.19)	8 (72.73)
		OR (95% CI)	0.83 (0.16, 4.40)	
		RR (95% CI)	0.87 (0.25, 2.99)	
		RD % (95% CI)	-3.46 (-35.47, 28.54)	
		p-value – Fisher's Exact Test	1.0000	
	Disturbance in attention	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Dizziness	Patients with any TEAEs	2 (9.52)	0 (0.00)
		Patients with no TEAEs	19 (90.48)	11 (100.00)
	Headache	Patients with any TEAEs	2 (9.52)	1 (9.09)
		Patients with no TEAEs	19 (90.48)	10 (90.91)
	Hyperammonaemic encephalopathy	Patients with any TEAEs	1 (4.76)	1 (9.09)
		Patients with no TEAEs	20 (95.24)	10 (90.91)
	Lethargy	Patients with any TEAEs	1 (4.76)	1 (9.09)
		Patients with no TEAEs	20 (95.24)	10 (90.91)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Any TEAEs by SOC and PT

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Nervous system disorders	Seizure	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Tonic convulsion	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
Psychiatric disorders	Total	Patients with any TEAEs	2 (9.52)	2 (18.18)
		Patients with no TEAEs	19 (90.48)	9 (81.82)
		OR (95% CI)	0.47 (0.06, 3.92)	
		RR (95% CI)	0.52 (0.08, 3.23)	
		RD % (95% CI)	-8.66 (-34.68, 17.36)	
		p-value – Fisher's Exact Test	0.5932	
	Behaviour disorder	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Generalised anxiety disorder	Patients with any TEAEs	0 (0.00)	1 (9.09)
		Patients with no TEAEs	21 (100.00)	10 (90.91)
	Mood altered	Patients with any TEAEs	0 (0.00)	1 (9.09)
		Patients with no TEAEs	21 (100.00)	10 (90.91)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-teae-soc.sas
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Any TEAEs by SOC and PT

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Psychiatric disorders	Panic attack	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
Respiratory, thoracic and mediastinal disorders	Total	Patients with any TEAEs	5 (23.81)	2 (18.18)
		Patients with no TEAEs	16 (76.19)	9 (81.82)
		OR (95% CI)	1.41 (0.23, 8.78)	
		RR (95% CI)	1.31 (0.30, 5.69)	
		RD % (95% CI)	5.63 (-23.55, 34.81)	
		p-value – Fisher's Exact Test	1.0000	
	Cough	Patients with any TEAEs	4 (19.05)	1 (9.09)
		Patients with no TEAEs	17 (80.95)	10 (90.91)
		OR (95% CI)	2.35 (0.23, 24.10)	
		RR (95% CI)	2.10 (0.27, 16.54)	
		RD % (95% CI)	9.96 (-13.93, 33.85)	
		p-value – Fisher's Exact Test	0.6367	
	Nasal congestion	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Any TEAEs by SOC and PT

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Respiratory, thoracic and mediastinal disorders	Nasal inflammation	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Oropharyngeal pain	Patients with any TEAEs	1 (4.76)	1 (9.09)
		Patients with no TEAEs	20 (95.24)	10 (90.91)
	Rhinorrhoea	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
Skin and subcutaneous tissue disorders	Total	Patients with any TEAEs	3 (14.29)	2 (18.18)
		Patients with no TEAEs	18 (85.71)	9 (81.82)
		OR (95% CI)	0.75 (0.11, 5.32)	
		RR (95% CI)	0.79 (0.15, 4.03)	
		RD % (95% CI)	-3.90 (-31.16, 23.37)	
		p-value – Fisher's Exact Test	1.0000	
	Dry skin	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Pruritus	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Any TEAEs by SOC and PT

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Skin and subcutaneous tissue disorders	Rash	Patients with any TEAEs	1 (4.76)	1 (9.09)
		Patients with no TEAEs	20 (95.24)	10 (90.91)
	Skin exfoliation	Patients with any TEAEs	0 (0.00)	1 (9.09)
		Patients with no TEAEs	21 (100.00)	10 (90.91)
Vascular disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Hypertension	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-teae-soc.sas
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4.9.1.10 Any severe TEAEs by SOC and PT

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Investigations	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Aspartate aminotransferase increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
Metabolism and nutrition disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Hyperammonaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
Psychiatric disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Panic attack	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=2; Placebo n=1.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-teae-soc.sas
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4.9.1.11 Treatment emergent SAEs by SOC and PT

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Gastrointestinal disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Vomiting	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
Metabolism and nutrition disorders	Total	Patients with any TEAEs	2 (9.52)	3 (27.27)
		Patients with no TEAEs	19 (90.48)	8 (72.73)
		OR (95% CI)	0.28 (0.04, 2.01)	
		RR (95% CI)	0.35 (0.07, 1.79)	
		RD % (95% CI)	-17.75 (-46.91, 11.41)	
		p-value – Fisher's Exact Test	0.3098	
	Hyperammonaemia	Patients with any TEAEs	2 (9.52)	3 (27.27)
		Patients with no TEAEs	19 (90.48)	8 (72.73)
		OR (95% CI)	0.28 (0.04, 2.01)	
		RR (95% CI)	0.35 (0.07, 1.79)	
		RD % (95% CI)	-17.75 (-46.91, 11.41)	
		p-value – Fisher's Exact Test	0.3098	

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=2; Placebo n=1.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-teae-soc.sas
Table Generation: 11SEP2023 2:37:36 PM

Treatment emergent SAEs by SOC and PT

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Nervous system disorders	Total	Patients with any TEAEs	1 (4.76)	1 (9.09)
		Patients with no TEAEs	20 (95.24)	10 (90.91)
		OR (95% CI)	0.50 (0.03, 8.85)	
		RR (95% CI)	0.52 (0.04, 7.59)	
		RD % (95% CI)	-4.33 (-23.61, 14.95)	
		p-value – Fisher's Exact Test	1.0000	
	Hyperammonaemic encephalopathy	Patients with any TEAEs	1 (4.76)	1 (9.09)
		Patients with no TEAEs	20 (95.24)	10 (90.91)
		OR (95% CI)	0.50 (0.03, 8.85)	
		RR (95% CI)	0.52 (0.04, 7.59)	
		RD % (95% CI)	-4.33 (-23.61, 14.95)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=2; Placebo n=1.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-teae-soc.sas
Table Generation: 11SEP2023 2:37:36 PM

4.9.2 Verträglichkeitsendpunkten (Gesamtraten bereinigt um krankheitsbezogene Ereignisse)

4.9.2.1 Patients with at least one TEAE while excluding disease associated adverse events

Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Patients with any TEAEs	18 (85.71)	10 (90.91)
Patients with no TEAEs	3 (14.29)	1 (9.09)
OR (95% CI)	0.60 (0.05, 6.56)	
RR (95% CI)	0.94 (0.73, 1.22)	
RD % (95% CI)	-5.19 (-27.84, 17.45)	
p-value – Fisher's Exact Test	1.0000	

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
Program: t-teae-sens.sas
Table Generation: 11SEP2023 2:39:22 PM

4.9.2.2 Patients with at least one severe TEAE while excluding disease associated adverse events

Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Patients with any severe TEAEs	1 (4.76)	0 (0.00)
Patients with no severe TEAEs	20 (95.24)	11 (100.00)
OR (95% CI)	1.68 (0.06, 44.77)	
RR (95% CI)	1.64 (0.07, 37.15)	
RD % (95% CI)	2.65 (-12.80, 18.10)	
p-value – Fisher's Exact Test	1.0000	

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
Program: t-teae-sens.sas
Table Generation: 11SEP2023 2:39:28 PM

4.9.2.3 Patients with at least one treatment emergent SAE while excluding disease associated adverse events

Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Patients with any treatment emergent SAEs	1 (4.76)	0 (0.00)
Patients with no treatment emergent SAEs	20 (95.24)	11 (100.00)
OR (95% CI)	1.68 (0.06, 44.77)	
RR (95% CI)	1.64 (0.07, 37.15)	
RD % (95% CI)	2.65 (-12.80, 18.10)	
p-value – Fisher's Exact Test	1.0000	

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
Program: t-teae-sens.sas
Table Generation: 11SEP2023 2:39:34 PM

4.9.2.4 Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Blood and lymphatic system disorders	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
		Patients with no TEAEs	19 (90.48)	11 (100.00)
	Anaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Iron deficiency anaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
Eye disorders	Total	Patients with any TEAEs	4 (19.05)	0 (0.00)
		Patients with no TEAEs	17 (80.95)	11 (100.00)
		OR (95% CI)	5.91 (0.29, 120.58)	
		RR (95% CI)	4.91 (0.29, 83.67)	
		RD % (95% CI)	16.29 (-4.01, 36.58)	
		p-value – Fisher's Exact Test	0.2720	
	Eye irritation	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
Program: t-teae-soc-sens.sas
Table Generation: 11SEP2023 2:55:16 PM

Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Eye disorders	Eye pain	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Eyelid oedema	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Ocular hyperaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
Gastrointestinal disorders	Total	Patients with any TEAEs	10 (47.62)	6 (54.55)
		Patients with no TEAEs	11 (52.38)	5 (45.45)
		OR (95% CI)	0.76 (0.18, 3.27)	
		RR (95% CI)	0.87 (0.43, 1.76)	
		RD % (95% CI)	-6.93 (-43.29, 29.43)	
		p-value – Fisher's Exact Test	1.0000	
	Abdominal discomfort	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Table Generation: 11SEP2023 2:55:16 PM

Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Gastrointestinal disorders	Abdominal pain	Patients with any TEAEs	1 (4.76)	3 (27.27)
		Patients with no TEAEs	20 (95.24)	8 (72.73)
		OR (95% CI)	0.13 (0.01, 1.48)	
		RR (95% CI)	0.17 (0.02, 1.49)	
		RD % (95% CI)	-22.51 (-50.36, 5.34)	
		p-value – Fisher's Exact Test	0.1055	
	Abdominal pain upper	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Anal rash	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Gastrointestinal disorders	Constipation	Patients with any TEAEs	3 (14.29)	1 (9.09)
		Patients with no TEAEs	18 (85.71)	10 (90.91)
		OR (95% CI)	1.67 (0.15, 18.22)	
		RR (95% CI)	1.57 (0.18, 13.39)	
		RD % (95% CI)	5.19 (-17.45, 27.84)	
		p-value – Fisher's Exact Test	1.0000	
	Diarrhoea	Patients with any TEAEs	1 (4.76)	1 (9.09)
		Patients with no TEAEs	20 (95.24)	10 (90.91)
	Haematochezia	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Gastrointestinal disorders	Nausea	Patients with any TEAEs	1 (4.76)	4 (36.36)
		Patients with no TEAEs	20 (95.24)	7 (63.64)
		OR (95% CI)	0.09 (0.01, 0.92)	
		RR (95% CI)	0.13 (0.02, 1.03)	
		RD % (95% CI)	-31.60 (-61.45, -1.75)	
		p-value – Fisher's Exact Test	0.0367 ***	
	Oral pain	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Vomiting	Patients with any TEAEs	6 (28.57)	3 (27.27)
		Patients with no TEAEs	15 (71.43)	8 (72.73)
		OR (95% CI)	1.07 (0.21, 5.44)	
		RR (95% CI)	1.05 (0.32, 3.40)	
		RD % (95% CI)	1.30 (-31.35, 33.95)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
General disorders and administration site conditions	Total	Patients with any TEAEs	7 (33.33)	0 (0.00)
		Patients with no TEAEs	14 (66.67)	11 (100.00)
		OR (95% CI)	11.90 (0.61, 230.84)	
		RR (95% CI)	8.18 (0.51, 131.22)	
		RD % (95% CI)	29.92 (7.12, 52.73)	
		p-value – Fisher's Exact Test	0.0664	
	Administration site extravasation	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Asthenia	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Illness	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Infusion site extravasation	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
General disorders and administration site conditions	Oedema peripheral	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Peripheral swelling	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Pyrexia	Patients with any TEAEs	4 (19.05)	0 (0.00)
		Patients with no TEAEs	17 (80.95)	11 (100.00)
		OR (95% CI)	5.91 (0.29, 120.58)	
		RR (95% CI)	4.91 (0.29, 83.67)	
		RD % (95% CI)	16.29 (-4.01, 36.58)	
		p-value – Fisher's Exact Test	0.2720	
	Swelling face	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
Hepatobiliary disorders	Total	Patients with any TEAEs	2 (9.52)	1 (9.09)
		Patients with no TEAEs	19 (90.48)	10 (90.91)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Hepatobiliary disorders	Cholelithiasis	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Hepatic cytolysis	Patients with any TEAEs	1 (4.76)	1 (9.09)
		Patients with no TEAEs	20 (95.24)	10 (90.91)
Immune system disorders	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
		Patients with no TEAEs	19 (90.48)	11 (100.00)
	Food allergy	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Hypersensitivity	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Infections and infestations	Total	Patients with any TEAEs	8 (38.10)	0 (0.00)
		Patients with no TEAEs	13 (61.90)	11 (100.00)
		OR (95% CI)	14.48 (0.75, 279.08)	
		RR (95% CI)	9.27 (0.58, 147.11)	
		RD % (95% CI)	34.47 (11.19, 57.75)	
		p-value – Fisher's Exact Test	0.0292 ***	
	Conjunctivitis	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Fungal skin infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Gastrointestinal viral infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Influenza	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Infections and infestations	Nasopharyngitis	Patients with any TEAEs	2 (9.52)	0 (0.00)
		Patients with no TEAEs	19 (90.48)	11 (100.00)
	Pharyngitis	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Respiratory syncytial virus infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Upper respiratory tract infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Viral infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Injury, poisoning and procedural complications	Total	Patients with any TEAEs	5 (23.81)	0 (0.00)
		Patients with no TEAEs	16 (76.19)	11 (100.00)
		OR (95% CI)	7.67 (0.39, 152.66)	
		RR (95% CI)	6.00 (0.36, 99.49)	
		RD % (95% CI)	20.83 (-0.50, 42.17)	
		p-value – Fisher's Exact Test	0.1378	
	Contusion	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Eye injury	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Fall	Patients with any TEAEs	2 (9.52)	0 (0.00)
		Patients with no TEAEs	19 (90.48)	11 (100.00)
	Procedural pain	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Injury, poisoning and procedural complications	Scratch	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
Investigations	Total	Patients with any TEAEs	5 (23.81)	2 (18.18)
		Patients with no TEAEs	16 (76.19)	9 (81.82)
		OR (95% CI)	1.41 (0.23, 8.78)	
		RR (95% CI)	1.31 (0.30, 5.69)	
		RD % (95% CI)	5.63 (-23.55, 34.81)	
		p-value – Fisher's Exact Test	1.0000	
	Activated partial thromboplastin time prolonged	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Amino acid level increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Blood alkaline phosphatase increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Investigations	Blood potassium decreased	Patients with any TEAEs	0 (0.00)	1 (9.09)
		Patients with no TEAEs	21 (100.00)	10 (90.91)
	Blood pressure increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Body temperature increased	Patients with any TEAEs	0 (0.00)	1 (9.09)
		Patients with no TEAEs	21 (100.00)	10 (90.91)
	Cardiac murmur	Patients with any TEAEs	1 (4.76)	1 (9.09)
		Patients with no TEAEs	20 (95.24)	10 (90.91)
	Electroencephalogram abnormal	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	International normalised ratio increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Prothrombin time prolonged	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Metabolism and nutrition disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Hypokalaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Vitamin D deficiency	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Vitamin K deficiency	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Zinc deficiency	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Musculoskeletal and connective tissue disorders	Total	Patients with any TEAEs	1 (4.76)	2 (18.18)
		Patients with no TEAEs	20 (95.24)	9 (81.82)
		OR (95% CI)	0.23 (0.02, 2.81)	
		RR (95% CI)	0.26 (0.03, 2.58)	
		RD % (95% CI)	-13.42 (-37.97, 11.13)	
		p-value – Fisher's Exact Test	0.2661	
	Arthralgia	Patients with any TEAEs	0 (0.00)	1 (9.09)
		Patients with no TEAEs	21 (100.00)	10 (90.91)
	Muscle spasms	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Osteochondrosis	Patients with any TEAEs	0 (0.00)	1 (9.09)
		Patients with no TEAEs	21 (100.00)	10 (90.91)
	Pain in extremity	Patients with any TEAEs	0 (0.00)	1 (9.09)
		Patients with no TEAEs	21 (100.00)	10 (90.91)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Nervous system disorders	Total	Patients with any TEAEs	4 (19.05)	2 (18.18)
		Patients with no TEAEs	17 (80.95)	9 (81.82)
		OR (95% CI)	1.06 (0.16, 6.94)	
		RR (95% CI)	1.05 (0.23, 4.85)	
		RD % (95% CI)	0.87 (-27.45, 29.18)	
		p-value – Fisher's Exact Test	1.0000	
	Disturbance in attention	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Dizziness	Patients with any TEAEs	2 (9.52)	0 (0.00)
		Patients with no TEAEs	19 (90.48)	11 (100.00)
	Headache	Patients with any TEAEs	2 (9.52)	1 (9.09)
		Patients with no TEAEs	19 (90.48)	10 (90.91)
	Lethargy	Patients with any TEAEs	1 (4.76)	1 (9.09)
		Patients with no TEAEs	20 (95.24)	10 (90.91)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
Program: t-teae-soc-sens.sas
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Psychiatric disorders	Total	Patients with any TEAEs	2 (9.52)	2 (18.18)
		Patients with no TEAEs	19 (90.48)	9 (81.82)
		OR (95% CI)	0.47 (0.06, 3.92)	
		RR (95% CI)	0.52 (0.08, 3.23)	
		RD % (95% CI)	-8.66 (-34.68, 17.36)	
		p-value – Fisher's Exact Test	0.5932	
	Behaviour disorder	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Generalised anxiety disorder	Patients with any TEAEs	0 (0.00)	1 (9.09)
		Patients with no TEAEs	21 (100.00)	10 (90.91)
	Mood altered	Patients with any TEAEs	0 (0.00)	1 (9.09)
		Patients with no TEAEs	21 (100.00)	10 (90.91)
	Panic attack	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Table Generation: 11SEP2023 2:55:16 PM

Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Respiratory, thoracic and mediastinal disorders	Total	Patients with any TEAEs	5 (23.81)	2 (18.18)
		Patients with no TEAEs	16 (76.19)	9 (81.82)
		OR (95% CI)	1.41 (0.23, 8.78)	
		RR (95% CI)	1.31 (0.30, 5.69)	
		RD % (95% CI)	5.63 (-23.55, 34.81)	
		p-value – Fisher's Exact Test	1.0000	
	Cough	Patients with any TEAEs	4 (19.05)	1 (9.09)
		Patients with no TEAEs	17 (80.95)	10 (90.91)
		OR (95% CI)	2.35 (0.23, 24.10)	
		RR (95% CI)	2.10 (0.27, 16.54)	
		RD % (95% CI)	9.96 (-13.93, 33.85)	
		p-value – Fisher's Exact Test	0.6367	
	Nasal congestion	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.

NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.

Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.

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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Respiratory, thoracic and mediastinal disorders	Nasal inflammation	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Oropharyngeal pain	Patients with any TEAEs	1 (4.76)	1 (9.09)
		Patients with no TEAEs	20 (95.24)	10 (90.91)
	Rhinorrhoea	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
Skin and subcutaneous tissue disorders	Total	Patients with any TEAEs	3 (14.29)	2 (18.18)
		Patients with no TEAEs	18 (85.71)	9 (81.82)
		OR (95% CI)	0.75 (0.11, 5.32)	
		RR (95% CI)	0.79 (0.15, 4.03)	
		RD % (95% CI)	-3.90 (-31.16, 23.37)	
		p-value – Fisher's Exact Test	1.0000	
	Dry skin	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Table Generation: 11SEP2023 2:55:16 PM

Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Skin and subcutaneous tissue disorders	Pruritus	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Rash	Patients with any TEAEs	1 (4.76)	1 (9.09)
		Patients with no TEAEs	20 (95.24)	10 (90.91)
	Skin exfoliation	Patients with any TEAEs	0 (0.00)	1 (9.09)
		Patients with no TEAEs	21 (100.00)	10 (90.91)
Vascular disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Hypertension	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
Program: t-teae-soc-sens.sas
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4.9.2.5 Any severe TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Psychiatric disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Panic attack	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=2; Placebo n=1.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
Program: t-teae-soc-sens.sas
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4.9.2.6 Treatment emergent SAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Gastrointestinal disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Vomiting	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=2; Placebo n=1.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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4.10 Subgruppenanalysen

4.10.1 Subgruppenanalysen für den Endpunkt Plasma-Arginin

4.10.1.1 Plasma arginine level by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.1561	
Male	Baseline	Absolute value	n (%)	12 (57.14)	7 (63.64)
			Geometric mean (log-scale SD)	356.80 (0.297)	490.20 (0.110)
	Week 6	Absolute value	n (%)	12 (57.14)	7 (63.64)
			Geometric mean (log-scale SD)	129.13 (0.432)	478.40 (0.200)
		Change from Baseline	n (%)	12 (57.14)	7 (63.64)
			Geometric Mean (log-scale SD)	0.36 (0.484)	0.98 (0.122)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.31	
			95% CI for GLS Mean Ratio [2]	0.20, 0.49	
			p-value MMRM [2]	<.0001 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.07	
			95% CI for SMD (Hedges' g)	0.02, 0.25	
			p-value WRS[3]	0.0003 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
Program: t-pd-cont-sub.sas
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1.4 Subgroup analyses
1.4.1 Plasma arginine
Plasma arginine level by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 12	Absolute value	n (%)	12 (57.14)	7 (63.64)
			Geometric mean (log-scale SD)	101.29 (0.469)	462.21 (0.141)
		Change from Baseline	n (%)	12 (57.14)	7 (63.64)
			Geometric Mean (log-scale SD)	0.28 (0.499)	0.94 (0.117)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.26	
			95% CI for GLS Mean Ratio [2]	0.16, 0.40	
			p-value MMRM [2]	<.0001 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.05	
			95% CI for SMD (Hedges' g)	0.01, 0.19	
			p-value WRS[3]	0.0005 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
Program: t-pd-cont-sub.sas
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1.4 Subgroup analyses
1.4.1 Plasma arginine
Plasma arginine level by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 18	Absolute value	n (%)	12 (57.14)	7 (63.64)
			Geometric mean (log-scale SD)	101.58 (0.502)	491.38 (0.188)
		Change from Baseline	n (%)	12 (57.14)	7 (63.64)
			Geometric Mean (log-scale SD)	0.28 (0.564)	1.00 (0.130)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.24	
			95% CI for GLS Mean Ratio [2]	0.15, 0.39	
			p-value MMRM [2]	<.0001 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.06	
			95% CI for SMD (Hedges' g)	0.01, 0.21	
			p-value WRS[3]	0.0003 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
Program: t-pd-cont-sub.sas
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1.4 Subgroup analyses
1.4.1 Plasma arginine
Plasma arginine level by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	12 (57.14)	7 (63.64)
			Geometric mean (log-scale SD)	94.14 (0.605)	424.61 (0.316)
		Change from Baseline	n (%)	12 (57.14)	7 (63.64)
			Geometric Mean (log-scale SD)	0.26 (0.613)	0.87 (0.371)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.26	
			95% CI for GLS Mean Ratio [2]	0.15, 0.46	
			p-value MMRM [2]	<.0001 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.10	
			95% CI for SMD (Hedges' g)	0.03, 0.33	
			p-value WRS[3]	0.0005 ***	
Female	Baseline	Absolute value	n (%)	9 (42.86)	4 (36.36)
			Geometric mean (log-scale SD)	350.30 (0.221)	423.34 (0.275)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
Program: t-pd-cont-sub.sas
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1.4 Subgroup analyses
1.4.1 Plasma arginine
Plasma arginine level by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 6	Absolute value	n (%)	8 (38.10)	4 (36.36)
			Geometric mean (log-scale SD)	111.75 (0.477)	490.25 (0.282)
		Change from Baseline	n (%)	8 (38.10)	4 (36.36)
			Geometric Mean (log-scale SD)	0.31 (0.384)	1.16 (0.056)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.24	
			95% CI for GLS Mean Ratio [2]	0.14, 0.40	
			p-value MMRM [2]	<.0001 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.03	
			95% CI for SMD (Hedges' g)	0.00, 0.22	
			p-value WRS[3]	0.0040 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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1.4 Subgroup analyses
1.4.1 Plasma arginine
Plasma arginine level by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	9 (42.86)	4 (36.36)
			Geometric mean (log-scale SD)	76.55 (0.219)	504.75 (0.262)
		Change from Baseline	n (%)	9 (42.86)	4 (36.36)
			Geometric Mean (log-scale SD)	0.22 (0.209)	1.19 (0.039)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.16	
			95% CI for GLS Mean Ratio [2]	0.13, 0.21	
			p-value MMRM [2]	<.0001 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.00	
			95% CI for SMD (Hedges' g)	0.00, 0.01	
			p-value WRS[3]	0.0028 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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1.4 Subgroup analyses
1.4.1 Plasma arginine
Plasma arginine level by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 18	Absolute value	n (%)	9 (42.86)	4 (36.36)
			Geometric mean (log-scale SD)	68.65 (0.274)	450.79 (0.265)
		Change from Baseline	n (%)	9 (42.86)	4 (36.36)
			Geometric Mean (log-scale SD)	0.20 (0.259)	1.06 (0.072)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.17	
			95% CI for GLS Mean Ratio [2]	0.12, 0.23	
			p-value MMRM [2]	<.0001 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.00	
			95% CI for SMD (Hedges' g)	0.00, 0.02	
			p-value WRS[3]	0.0028 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
Program: t-pd-cont-sub.sas
Table Generation: 11SEP2023 9:14:15 AM

1.4 Subgroup analyses
1.4.1 Plasma arginine
Plasma arginine level by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	9 (42.86)	4 (36.36)
			Geometric mean (log-scale SD)	76.99 (0.161)	429.88 (0.205)
		Change from Baseline	n (%)	9 (42.86)	4 (36.36)
			Geometric Mean (log-scale SD)	0.22 (0.259)	1.02 (0.185)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.19	
			95% CI for GLS Mean Ratio [2]	0.15, 0.25	
			p-value MMRM [2]	<.0001 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.00	
			95% CI for SMD (Hedges' g)	0.00, 0.01	
			p-value WRS[3]	0.0028 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.1.2 Plasma arginine level by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.1286	
<10.5 years old at screening	Baseline	Absolute value	n (%)	12 (57.14)	4 (36.36)
			Geometric mean (log-scale SD)	329.80 (0.245)	447.35 (0.091)
	Week 6	Absolute value	n (%)	12 (57.14)	4 (36.36)
			Geometric mean (log-scale SD)	136.88 (0.531)	432.25 (0.219)
		Change from Baseline	n (%)	12 (57.14)	4 (36.36)
			Geometric Mean (log-scale SD)	0.42 (0.402)	0.97 (0.178)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.51	
			95% CI for GLS Mean Ratio [2]	0.30, 0.88	
			p-value MMRM [2]	0.0188 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.21	
			95% CI for SMD (Hedges' g)	0.06, 0.74	
			p-value WRS[3]	0.0044 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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Plasma arginine level by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 12	Absolute value	n (%)	12 (57.14)	4 (36.36)
			Geometric mean (log-scale SD)	92.69 (0.494)	473.52 (0.160)
		Change from Baseline	n (%)	12 (57.14)	4 (36.36)
			Geometric Mean (log-scale SD)	0.28 (0.447)	1.06 (0.089)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.32	
			95% CI for GLS Mean Ratio [2]	0.17, 0.59	
			p-value MMRM [2]	0.0014 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.10	
			95% CI for SMD (Hedges' g)	0.03, 0.43	
			p-value WRS[3]	0.0022 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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Plasma arginine level by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 18	Absolute value	n (%)	12 (57.14)	4 (36.36)
			Geometric mean (log-scale SD)	92.94 (0.539)	475.20 (0.214)
		Change from Baseline	n (%)	12 (57.14)	4 (36.36)
			Geometric Mean (log-scale SD)	0.28 (0.515)	1.06 (0.143)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.32	
			95% CI for GLS Mean Ratio [2]	0.16, 0.63	
			p-value MMRM [2]	0.0031 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.14	
			95% CI for SMD (Hedges' g)	0.04, 0.53	
			p-value WRS[3]	0.0022 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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Plasma arginine level by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	12 (57.14)	4 (36.36)
			Geometric mean (log-scale SD)	98.08 (0.555)	453.08 (0.095)
		Change from Baseline	n (%)	12 (57.14)	4 (36.36)
			Geometric Mean (log-scale SD)	0.30 (0.470)	1.01 (0.036)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.35	
			95% CI for GLS Mean Ratio [2]	0.19, 0.65	
			p-value MMRM [2]	0.0023 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.12	
			95% CI for SMD (Hedges' g)	0.03, 0.48	
			p-value WRS[3]	0.0011 ***	
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	9 (42.86)	7 (63.64)
			Geometric mean (log-scale SD)	389.05 (0.265)	474.98 (0.231)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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Plasma arginine level by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 6	Absolute value	n (%)	8 (38.10)	7 (63.64)
			Geometric mean (log-scale SD)	102.39 (0.187)	514.09 (0.208)
		Change from Baseline	n (%)	8 (38.10)	7 (63.64)
			Geometric Mean (log-scale SD)	0.25 (0.333)	1.08 (0.088)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.21	
			95% CI for GLS Mean Ratio [2]	0.16, 0.26	
			p-value MMRM [2]	<.0001 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.00	
			95% CI for SMD (Hedges' g)	0.00, 0.01	
			p-value WRS[3]	0.0003 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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Plasma arginine level by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	9 (42.86)	7 (63.64)
			Geometric mean (log-scale SD)	86.16 (0.250)	479.38 (0.211)
		Change from Baseline	n (%)	9 (42.86)	7 (63.64)
			Geometric Mean (log-scale SD)	0.22 (0.345)	1.01 (0.182)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.19	
			95% CI for GLS Mean Ratio [2]	0.15, 0.25	
			p-value MMRM [2]	<.0001 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.00	
			95% CI for SMD (Hedges' g)	0.00, 0.02	
			p-value WRS[3]	0.0002 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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Plasma arginine level by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 18	Absolute value	n (%)	9 (42.86)	7 (63.64)
			Geometric mean (log-scale SD)	77.30 (0.315)	476.79 (0.225)
		Change from Baseline	n (%)	9 (42.86)	7 (63.64)
			Geometric Mean (log-scale SD)	0.20 (0.388)	1.00 (0.097)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.17	
			95% CI for GLS Mean Ratio [2]	0.13, 0.23	
			p-value MMRM [2]	<.0001 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.00	
			95% CI for SMD (Hedges' g)	0.00, 0.03	
			p-value WRS[3]	0.0002 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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Plasma arginine level by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	9 (42.86)	7 (63.64)
			Geometric mean (log-scale SD)	72.90 (0.273)	412.05 (0.336)
		Change from Baseline	n (%)	9 (42.86)	7 (63.64)
			Geometric Mean (log-scale SD)	0.19 (0.406)	0.87 (0.394)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.19	
			95% CI for GLS Mean Ratio [2]	0.13, 0.26	
			p-value MMRM [2]	<.0001 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.01	
			95% CI for SMD (Hedges' g)	0.00, 0.06	
			p-value WRS[3]	0.0003 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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4.10.1.3 Plasma arginine level by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.5566	
US	Baseline	Absolute value	n (%)	8 (38.10)	6 (54.55)
			Geometric mean (log-scale SD)	333.45 (0.256)	465.26 (0.092)
	Week 6	Absolute value	n (%)	8 (38.10)	6 (54.55)
			Geometric mean (log-scale SD)	97.60 (0.222)	459.31 (0.203)
		Change from Baseline	n (%)	8 (38.10)	6 (54.55)
			Geometric Mean (log-scale SD)	0.29 (0.254)	0.99 (0.131)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.23	
			95% CI for GLS Mean Ratio [2]	0.18, 0.31	
			p-value MMRM [2]	<.0001 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.00	
			95% CI for SMD (Hedges' g)	0.00, 0.03	
			p-value WRS[3]	0.0007 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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Plasma arginine level by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 12	Absolute value	n (%)	8 (38.10)	6 (54.55)
			Geometric mean (log-scale SD)	78.76 (0.217)	472.28 (0.151)
		Change from Baseline	n (%)	8 (38.10)	6 (54.55)
			Geometric Mean (log-scale SD)	0.24 (0.298)	1.02 (0.133)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.18	
			95% CI for GLS Mean Ratio [2]	0.14, 0.24	
			p-value MMRM [2]	<.0001 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.00	
			95% CI for SMD (Hedges' g)	0.00, 0.02	
			p-value WRS[3]	0.0007 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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Plasma arginine level by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 18	Absolute value	n (%)	8 (38.10)	6 (54.55)
			Geometric mean (log-scale SD)	73.90 (0.330)	480.81 (0.168)
		Change from Baseline	n (%)	8 (38.10)	6 (54.55)
			Geometric Mean (log-scale SD)	0.22 (0.428)	1.03 (0.131)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.17	
			95% CI for GLS Mean Ratio [2]	0.12, 0.24	
			p-value MMRM [2]	<.0001 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.00	
			95% CI for SMD (Hedges' g)	0.00, 0.05	
			p-value WRS[3]	0.0007 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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Plasma arginine level by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	8 (38.10)	6 (54.55)
			Geometric mean (log-scale SD)	77.84 (0.210)	447.62 (0.141)
		Change from Baseline	n (%)	8 (38.10)	6 (54.55)
			Geometric Mean (log-scale SD)	0.23 (0.325)	0.96 (0.089)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.19	
			95% CI for GLS Mean Ratio [2]	0.15, 0.25	
			p-value MMRM [2]	<.0001 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.00	
			95% CI for SMD (Hedges' g)	0.00, 0.02	
			p-value WRS[3]	0.0007 ***	
Non-US	Baseline	Absolute value	n (%)	13 (61.90)	5 (45.45)
			Geometric mean (log-scale SD)	367.28 (0.267)	464.13 (0.279)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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Plasma arginine level by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 6	Absolute value	n (%)	12 (57.14)	5 (45.45)
			Geometric mean (log-scale SD)	141.32 (0.500)	512.30 (0.246)
		Change from Baseline	n (%)	12 (57.14)	5 (45.45)
			Geometric Mean (log-scale SD)	0.38 (0.518)	1.10 (0.116)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.30	
			95% CI for GLS Mean Ratio [2]	0.18, 0.51	
			p-value MMRM [2]	0.0002 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.08	
			95% CI for SMD (Hedges' g)	0.02, 0.33	
			p-value WRS[3]	0.0006 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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Plasma arginine level by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	13 (61.90)	5 (45.45)
			Geometric mean (log-scale SD)	97.41 (0.471)	483.27 (0.239)
		Change from Baseline	n (%)	13 (61.90)	5 (45.45)
			Geometric Mean (log-scale SD)	0.27 (0.479)	1.04 (0.185)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.23	
			95% CI for GLS Mean Ratio [2]	0.14, 0.38	
			p-value MMRM [2]	<.0001 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.04	
			95% CI for SMD (Hedges' g)	0.01, 0.19	
			p-value WRS[3]	0.0009 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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Plasma arginine level by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 18	Absolute value	n (%)	13 (61.90)	5 (45.45)
			Geometric mean (log-scale SD)	94.20 (0.508)	470.76 (0.274)
		Change from Baseline	n (%)	13 (61.90)	5 (45.45)
			Geometric Mean (log-scale SD)	0.26 (0.529)	1.01 (0.099)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.23	
			95% CI for GLS Mean Ratio [2]	0.13, 0.39	
			p-value MMRM [2]	<.0001 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.05	
			95% CI for SMD (Hedges' g)	0.01, 0.23	
			p-value WRS[3]	0.0005 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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Plasma arginine level by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	13 (61.90)	5 (45.45)
			Geometric mean (log-scale SD)	92.07 (0.576)	402.51 (0.386)
		Change from Baseline	n (%)	13 (61.90)	5 (45.45)
			Geometric Mean (log-scale SD)	0.25 (0.583)	0.87 (0.481)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.26	
			95% CI for GLS Mean Ratio [2]	0.14, 0.49	
			p-value MMRM [2]	0.0003 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.10	
			95% CI for SMD (Hedges' g)	0.03, 0.38	
			p-value WRS[3]	0.0016 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.1.4 Plasma arginine level by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.7563	
I	Baseline	Absolute value	n (%)	9 (42.86)	5 (45.45)
			Geometric mean (log-scale SD)	355.20 (0.240)	433.26 (0.259)
	Week 6	Absolute value	n (%)	8 (38.10)	5 (45.45)
			Geometric mean (log-scale SD)	136.26 (0.632)	453.99 (0.320)
		Change from Baseline	n (%)	8 (38.10)	5 (45.45)
			Geometric Mean (log-scale SD)	0.37 (0.535)	1.05 (0.164)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.38	
			95% CI for GLS Mean Ratio [2]	0.21, 0.69	
			p-value MMRM [2]	0.0042 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.15	
			95% CI for SMD (Hedges' g)	0.04, 0.58	
			p-value WRS[3]	0.0031 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
Program: t-pd-cont-sub.sas
Table Generation: 11SEP2023 9:14:32 AM

Plasma arginine level by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 12	Absolute value	n (%)	9 (42.86)	5 (45.45)
			Geometric mean (log-scale SD)	99.94 (0.561)	477.37 (0.263)
		Change from Baseline	n (%)	9 (42.86)	5 (45.45)
			Geometric Mean (log-scale SD)	0.28 (0.510)	1.10 (0.134)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.28	
			95% CI for GLS Mean Ratio [2]	0.15, 0.52	
			p-value MMRM [2]	0.0010 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.10	
			95% CI for SMD (Hedges' g)	0.02, 0.41	
			p-value WRS[3]	0.0020 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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Table Generation: 11SEP2023 9:14:32 AM

Plasma arginine level by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 18	Absolute value	n (%)	9 (42.86)	5 (45.45)
			Geometric mean (log-scale SD)	94.96 (0.618)	432.55 (0.254)
		Change from Baseline	n (%)	9 (42.86)	5 (45.45)
			Geometric Mean (log-scale SD)	0.27 (0.601)	1.00 (0.097)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.29	
			95% CI for GLS Mean Ratio [2]	0.15, 0.59	
			p-value MMRM [2]	0.0028 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.14	
			95% CI for SMD (Hedges' g)	0.04, 0.54	
			p-value WRS[3]	0.0040 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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Table Generation: 11SEP2023 9:14:32 AM

Plasma arginine level by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	9 (42.86)	5 (45.45)
			Geometric mean (log-scale SD)	86.09 (0.603)	427.03 (0.190)
		Change from Baseline	n (%)	9 (42.86)	5 (45.45)
			Geometric Mean (log-scale SD)	0.24 (0.616)	0.99 (0.159)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.27	
			95% CI for GLS Mean Ratio [2]	0.13, 0.57	
			p-value MMRM [2]	0.0031 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.14	
			95% CI for SMD (Hedges' g)	0.04, 0.54	
			p-value WRS[3]	0.0040 ***	
≥ II	Baseline	Absolute value	n (%)	12 (57.14)	6 (54.55)
			Geometric mean (log-scale SD)	353.11 (0.286)	492.72 (0.091)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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Table Generation: 11SEP2023 9:14:32 AM

Plasma arginine level by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 6	Absolute value	n (%)	12 (57.14)	6 (54.55)
			Geometric mean (log-scale SD)	113.14 (0.267)	507.96 (0.086)
		Change from Baseline	n (%)	12 (57.14)	6 (54.55)
			Geometric Mean (log-scale SD)	0.32 (0.380)	1.03 (0.115)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.23	
			95% CI for GLS Mean Ratio [2]	0.17, 0.30	
			p-value MMRM [2]	<.0001 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.00	
			95% CI for SMD (Hedges' g)	0.00, 0.03	
			p-value WRS[3]	0.0001 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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Plasma arginine level by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	12 (57.14)	6 (54.55)
			Geometric mean (log-scale SD)	82.93 (0.215)	477.14 (0.116)
		Change from Baseline	n (%)	12 (57.14)	6 (54.55)
			Geometric Mean (log-scale SD)	0.23 (0.328)	0.97 (0.148)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.18	
			95% CI for GLS Mean Ratio [2]	0.14, 0.23	
			p-value MMRM [2]	<.0001 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.00	
			95% CI for SMD (Hedges' g)	0.00, 0.01	
			p-value WRS[3]	0.0001 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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Plasma arginine level by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 18	Absolute value	n (%)	12 (57.14)	6 (54.55)
			Geometric mean (log-scale SD)	79.65 (0.292)	515.95 (0.141)
		Change from Baseline	n (%)	12 (57.14)	6 (54.55)
			Geometric Mean (log-scale SD)	0.23 (0.394)	1.05 (0.128)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.16	
			95% CI for GLS Mean Ratio [2]	0.12, 0.21	
			p-value MMRM [2]	<.0001 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.00	
			95% CI for SMD (Hedges' g)	0.00, 0.02	
			p-value WRS[3]	0.0001 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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Plasma arginine level by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	12 (57.14)	6 (54.55)
			Geometric mean (log-scale SD)	86.58 (0.373)	426.11 (0.341)
		Change from Baseline	n (%)	12 (57.14)	6 (54.55)
			Geometric Mean (log-scale SD)	0.25 (0.404)	0.86 (0.411)
			GLS Mean Ratio (Pegzilarginase-Placebo) [2]	0.21	
			95% CI for GLS Mean Ratio [2]	0.14, 0.31	
			p-value MMRM [2]	<.0001 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.02	
			95% CI for SMD (Hedges' g)	0.00, 0.11	
			p-value WRS[3]	0.0004 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; GLS = Geometric
Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.2 Subgruppenanalysen für den Endpunkt 2MWT

4.10.2.1 2MWT by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.9025	
Male	Baseline	Absolute value	n (%)	12 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	106.92 (52.351)	89.57 (47.162)
	Week 12	Absolute value	n (%)	10 (83.33)	6 (85.71)
			Number of patients with missing data: n (%)	2 (16.67)	1 (14.29)
			Mean (SD)	108.70 (68.307)	84.17 (58.857)
		Change from Baseline	n (%)	10 (83.33)	6 (85.71)
			Number of patients with missing data: n (%)	2 (16.67)	1 (14.29)
			LS Mean Change from Baseline (SE) [2]	7.53 (8.624)	-3.42 (11.078)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	10.95 (14.062)	
			95% CI for LS Mean Difference [2]	-19.45, 41.34	
			p-value MMRM [2]	0.4502	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.36	
			95% CI for SMD (Hedges' g)	-0.66, 1.39	
			p-value WRS[3]	0.9578	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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1.4.2 2MWT
2MWT by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	11 (91.67)	6 (85.71)
			Number of patients with missing data: n (%)	1 (8.33)	1 (14.29)
			Mean (SD)	111.36 (52.081)	91.67 (49.172)
		Change from Baseline	n (%)	11 (91.67)	6 (85.71)
			Number of patients with missing data: n (%)	1 (8.33)	1 (14.29)
			LS Mean Change from Baseline (SE) [2]	8.72 (6.093)	4.08 (8.257)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	4.64 (10.308)	
			95% CI for LS Mean Difference [2]	-17.49, 26.76	
			p-value MMRM [2]	0.6597	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.21	
			95% CI for SMD (Hedges' g)	-0.79, 1.21	
			p-value WRS[3]	0.4489	
Female	Baseline	Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	112.13 (64.150)	118.00 (53.572)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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1.4.2 2MWT
2MWT by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	129.63 (28.908)	104.00 (56.059)
		Change from Baseline	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	4.08 (9.582)	-14.23 (13.339)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	18.31 (16.423)	
			95% CI for LS Mean Difference [2]	-19.00, 55.62	
			p-value MMRM [2]	0.2946	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.61	
			95% CI for SMD (Hedges' g)	-0.65, 1.87	
			p-value WRS[3]	0.5273	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
Program: t-qs-cont-sub.sas
Table Generation: 11SEP2023 1:16:51 PM

1.4.2 2MWT
2MWT by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	121.33 (54.062)	118.25 (56.900)
		Change from Baseline	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	3.98 (12.584)	0.02 (17.730)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.96 (21.734)	
			95% CI for LS Mean Difference [2]	-44.75, 52.67	
			p-value MMRM [2]	0.8593	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.10	
			95% CI for SMD (Hedges' g)	-1.10, 1.30	
			p-value WRS[3]	1.0000	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.2.2 2MWT by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.6110	
<10.5 years old at screening	Baseline	Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	111.82 (47.480)	97.00 (38.652)
	Week 12	Absolute value	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	109.70 (45.446)	93.75 (51.539)
		Change from Baseline	n (%)	9 (75.00)	4 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	2.35 (8.945)	-4.56 (13.764)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	6.91 (16.460)	
			95% CI for LS Mean Difference [2]	-29.66, 43.48	
			p-value MMRM [2]	0.6834	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.23	
			95% CI for SMD (Hedges' g)	-0.96, 1.41	
			p-value WRS[3]	0.7105	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

NOTE: Median age used as cut-off point.

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2MWT by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	120.45 (41.322)	87.25 (41.015)
		Change from Baseline	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	10.41 (10.165)	-11.06 (16.087)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	21.47 (19.079)	
			95% CI for LS Mean Difference [2]	-20.80, 63.75	
			p-value MMRM [2]	0.2856	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.59	
			95% CI for SMD (Hedges' g)	-0.59, 1.77	
			p-value WRS[3]	0.3896	
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	105.56 (67.404)	101.57 (56.976)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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2MWT by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	8 (88.89)	6 (85.71)
			Number of patients with missing data: n (%)	1 (11.11)	1 (14.29)
			Mean (SD)	128.38 (65.082)	91.00 (62.779)
		Change from Baseline	n (%)	8 (88.89)	6 (85.71)
			Number of patients with missing data: n (%)	1 (11.11)	1 (14.29)
			LS Mean Change from Baseline (SE) [2]	9.35 (10.445)	-10.87 (12.202)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	20.22 (16.065)	
			95% CI for LS Mean Difference [2]	-14.73, 55.16	
			p-value MMRM [2]	0.2318	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.61	
			95% CI for SMD (Hedges' g)	-0.47, 1.70	
			p-value WRS[3]	0.2824	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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2MWT by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	9 (100.00)	6 (85.71)
			Number of patients with missing data: n (%)	0 (0.00)	1 (14.29)
			Mean (SD)	110.22 (64.620)	112.33 (58.209)
		Change from Baseline	n (%)	9 (100.00)	6 (85.71)
			Number of patients with missing data: n (%)	0 (0.00)	1 (14.29)
			LS Mean Change from Baseline (SE) [2]	4.51 (6.519)	10.46 (7.999)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-5.96 (10.311)	
			95% CI for LS Mean Difference [2]	-28.42, 16.50	
			p-value MMRM [2]	0.5740	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.27	
			95% CI for SMD (Hedges' g)	-1.31, 0.76	
			p-value WRS[3]	0.7982	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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4.10.2.3 2MWT by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.8951	
US	Baseline	Absolute value	n (%)	7 (87.50)	6 (100.00)
			Number of patients with missing data: n (%)	1 (12.50)	0 (0.00)
			Mean (SD)	110.29 (46.860)	90.67 (50.548)
	Week 12	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	117.63 (49.077)	95.67 (52.561)
		Change from Baseline	n (%)	7 (87.50)	6 (100.00)
			Number of patients with missing data: n (%)	1 (12.50)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	8.87 (8.836)	5.15 (9.565)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.71 (13.207)	
			95% CI for LS Mean Difference [2]	-25.73, 33.16	
			p-value MMRM [2]	0.7843	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.14	
			95% CI for SMD (Hedges' g)	-0.95, 1.23	
			p-value WRS[3]	0.4441	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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2MWT by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	130.13 (41.591)	94.67 (50.887)
		Change from Baseline	n (%)	7 (87.50)	6 (100.00)
			Number of patients with missing data: n (%)	1 (12.50)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	16.87 (11.910)	4.15 (12.880)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	12.71 (17.680)	
			95% CI for LS Mean Difference [2]	-27.16, 52.58	
			p-value MMRM [2]	0.4900	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.35	
			95% CI for SMD (Hedges' g)	-0.75, 1.45	
			p-value WRS[3]	0.7593	
Non-US	Baseline	Absolute value	n (%)	13 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	108.31 (61.840)	111.00 (50.274)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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2MWT by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	10 (76.92)	4 (80.00)
			Number of patients with missing data: n (%)	3 (23.08)	1 (20.00)
			Mean (SD)	118.30 (60.485)	86.75 (67.549)
		Change from Baseline	n (%)	10 (76.92)	4 (80.00)
			Number of patients with missing data: n (%)	3 (23.08)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	3.40 (9.559)	-25.80 (15.257)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	29.20 (18.007)	
			95% CI for LS Mean Difference [2]	-10.07, 68.47	
			p-value MMRM [2]	0.1310	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.87	
			95% CI for SMD (Hedges' g)	-0.34, 2.08	
			p-value WRS[3]	0.0799	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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2MWT by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	12 (92.31)	4 (80.00)
			Number of patients with missing data: n (%)	1 (7.69)	1 (20.00)
			Mean (SD)	106.33 (57.345)	113.75 (56.794)
		Change from Baseline	n (%)	12 (92.31)	4 (80.00)
			Number of patients with missing data: n (%)	1 (7.69)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	1.00 (7.113)	1.20 (12.290)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.20 (14.214)	
			95% CI for LS Mean Difference [2]	-30.89, 30.49	
			p-value MMRM [2]	0.9891	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.01	
			95% CI for SMD (Hedges' g)	-1.14, 1.12	
			p-value WRS[3]	0.7516	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.2.4 2MWT by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.6809	
I	Baseline	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	141.63 (37.702)	137.20 (31.507)
	Week 12	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	143.50 (43.788)	132.40 (23.234)
		Change from Baseline	n (%)	7 (77.78)	5 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	9.14 (10.265)	-5.40 (12.146)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	14.54 (15.906)	
			95% CI for LS Mean Difference [2]	-20.98, 50.05	
			p-value MMRM [2]	0.3826	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.47	
			95% CI for SMD (Hedges' g)	-0.70, 1.64	
			p-value WRS[3]	0.8447	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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2MWT by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	144.63 (33.645)	140.40 (15.209)
		Change from Baseline	n (%)	7 (77.78)	5 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	4.14 (6.443)	2.60 (7.624)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.54 (9.986)	
			95% CI for LS Mean Difference [2]	-20.97, 24.04	
			p-value MMRM [2]	0.8810	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.08	
			95% CI for SMD (Hedges' g)	-1.07, 1.23	
			p-value WRS[3]	0.8763	
≥ II	Baseline	Absolute value	n (%)	12 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	87.25 (56.361)	68.83 (38.196)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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2MWT by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	10 (83.33)	5 (83.33)
			Number of patients with missing data: n (%)	2 (16.67)	1 (16.67)
			Mean (SD)	97.60 (54.775)	51.80 (48.200)
		Change from Baseline	n (%)	10 (83.33)	5 (83.33)
			Number of patients with missing data: n (%)	2 (16.67)	1 (16.67)
			LS Mean Change from Baseline (SE) [2]	4.89 (9.014)	-12.76 (12.999)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	17.65 (16.048)	
			95% CI for LS Mean Difference [2]	-16.93, 52.23	
			p-value MMRM [2]	0.2908	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.56	
			95% CI for SMD (Hedges' g)	-0.54, 1.65	
			p-value WRS[3]	0.3866	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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2MWT by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	12 (100.00)	5 (83.33)
			Number of patients with missing data: n (%)	0 (0.00)	1 (16.67)
			Mean (SD)	96.67 (53.965)	64.20 (44.880)
		Change from Baseline	n (%)	12 (100.00)	5 (83.33)
			Number of patients with missing data: n (%)	0 (0.00)	1 (16.67)
			LS Mean Change from Baseline (SE) [2]	10.28 (9.249)	-0.36 (14.510)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	10.65 (17.348)	
			95% CI for LS Mean Difference [2]	-26.44, 47.73	
			p-value MMRM [2]	0.5489	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.30	
			95% CI for SMD (Hedges' g)	-0.75, 1.35	
			p-value WRS[3]	0.7812	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.2.5 2MWT responders ≥ 9% improvement by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Gender, p-value Chi-Square[1]	0.5042	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (14.29)
		Non-Responders [2]	9 (75.00)	6 (85.71)
		Responders	3 (25.00)	1 (14.29)
		OR (95% CI)	2.00 (0.17, 24.07)	
		RR (95% CI)	1.75 (0.22, 13.76)	
		RD % (95% CI)	10.71 (-24.95, 46.38)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	1 (14.29)
		Non-Responders [2]	8 (66.67)	6 (85.71)
		Responders	4 (33.33)	1 (14.29)
		OR (95% CI)	3.00 (0.26, 34.20)	
		RR (95% CI)	2.33 (0.32, 16.95)	
		RD % (95% CI)	19.05 (-18.15, 56.24)	
		p-value – Fisher's Exact Test	0.6027	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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2MWT responders ≥ 9% improvement by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (22.22)	0 (0.00)
		Non-Responders [2]	6 (66.67)	3 (75.00)
		Responders	3 (33.33)	1 (25.00)
		OR (95% CI)	1.50 (0.11, 21.31)	
		RR (95% CI)	1.33 (0.19, 9.21)	
		RD % (95% CI)	8.33 (-44.10, 60.77)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	7 (77.78)	3 (75.00)
		Responders	2 (22.22)	1 (25.00)
		OR (95% CI)	0.86 (0.05, 13.48)	
		RR (95% CI)	0.89 (0.11, 7.20)	
		RD % (95% CI)	-2.78 (-53.16, 47.60)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.2.6 2MWT responders ≥ 9% improvement by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Age Group, p-value Chi-Square[1]	0.9779	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (25.00)	0 (0.00)
		Non-Responders [2]	10 (83.33)	3 (75.00)
		Responders	2 (16.67)	1 (25.00)
		OR (95% CI)	0.60 (0.04, 9.16)	
		RR (95% CI)	0.67 (0.08, 5.54)	
		RD % (95% CI)	-8.33 (-55.72, 39.05)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	9 (75.00)	4 (100.00)
		Responders	3 (25.00)	0 (0.00)
		OR (95% CI)	3.32 (0.14, 78.81)	
		RR (95% CI)	2.69 (0.17, 43.31)	
		RD % (95% CI)	16.92 (-18.75, 52.60)	
		p-value – Fisher's Exact Test	0.5286	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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2MWT responders ≥ 9% improvement by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (14.29)
		Non-Responders [2]	5 (55.56)	6 (85.71)
		Responders	4 (44.44)	1 (14.29)
		OR (95% CI)	4.80 (0.40, 58.01)	
		RR (95% CI)	3.11 (0.44, 22.00)	
		RD % (95% CI)	30.16 (-11.38, 71.70)	
		p-value – Fisher's Exact Test	0.3077	
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	1 (14.29)
		Non-Responders [2]	6 (66.67)	5 (71.43)
		Responders	3 (33.33)	2 (28.57)
		OR (95% CI)	1.25 (0.15, 10.70)	
		RR (95% CI)	1.17 (0.26, 5.19)	
		RD % (95% CI)	4.76 (-40.72, 50.24)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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Table Generation: 11SEP2023 12:13:07 PM

4.10.2.7 2MWT responders ≥ 9% improvement by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Region, p-value Chi-Square[1]	0.6201	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (12.50)	0 (0.00)
		Non-Responders [2]	6 (75.00)	4 (66.67)
		Responders	2 (25.00)	2 (33.33)
		OR (95% CI)	0.67 (0.06, 6.87)	
		RR (95% CI)	0.75 (0.14, 3.90)	
		RD % (95% CI)	-8.33 (-56.53, 39.87)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (12.50)	0 (0.00)
		Non-Responders [2]	5 (62.50)	5 (83.33)
		Responders	3 (37.50)	1 (16.67)
		OR (95% CI)	3.00 (0.23, 39.61)	
		RR (95% CI)	2.25 (0.30, 16.63)	
		RD % (95% CI)	20.83 (-24.05, 65.72)	
		p-value – Fisher's Exact Test	0.5804	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
Table Generation: 11SEP2023 12:13:13 PM

2MWT responders ≥ 9% improvement by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (23.08)	1 (20.00)
		Non-Responders [2]	9 (69.23)	5 (100.00)
		Responders	4 (30.77)	0 (0.00)
		OR (95% CI)	5.21 (0.23, 116.21)	
		RR (95% CI)	3.86 (0.24, 60.99)	
		RD % (95% CI)	23.81 (-9.17, 56.79)	
		p-value – Fisher's Exact Test	0.2778	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (7.69)	1 (20.00)
		Non-Responders [2]	10 (76.92)	4 (80.00)
		Responders	3 (23.08)	1 (20.00)
		OR (95% CI)	1.20 (0.09, 15.26)	
		RR (95% CI)	1.15 (0.15, 8.65)	
		RD % (95% CI)	3.08 (-38.80, 44.96)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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4.10.2.8 2MWT responders ≥ 9% improvement by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.3206	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (22.22)	0 (0.00)
		Non-Responders [2]	7 (77.78)	4 (80.00)
		Responders	2 (22.22)	1 (20.00)
		OR (95% CI)	1.14 (0.08, 16.95)	
		RR (95% CI)	1.11 (0.13, 9.42)	
		RD % (95% CI)	2.22 (-42.13, 46.57)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (22.22)	0 (0.00)
		Non-Responders [2]	8 (88.89)	4 (80.00)
		Responders	1 (11.11)	1 (20.00)
		OR (95% CI)	0.50 (0.02, 10.25)	
		RR (95% CI)	0.56 (0.04, 7.09)	
		RD % (95% CI)	-8.89 (-49.52, 31.74)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
Table Generation: 11SEP2023 12:13:20 PM

2MWT responders ≥ 9% improvement by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (16.67)
		Non-Responders [2]	8 (66.67)	5 (83.33)
		Responders	4 (33.33)	1 (16.67)
		OR (95% CI)	2.50 (0.21, 29.25)	
		RR (95% CI)	2.00 (0.28, 14.20)	
		RD % (95% CI)	16.67 (-23.34, 56.67)	
		p-value – Fisher's Exact Test	0.6148	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	1 (16.67)
		Non-Responders [2]	7 (58.33)	5 (83.33)
		Responders	5 (41.67)	1 (16.67)
		OR (95% CI)	3.57 (0.31, 40.75)	
		RR (95% CI)	2.50 (0.37, 16.89)	
		RD % (95% CI)	25.00 (-15.83, 65.83)	
		p-value – Fisher's Exact Test	0.6000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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4.10.2.9 2MWT responders ≥ 15% improvement by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Gender, p-value Chi-Square[1]	0.5042	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (14.29)
		Non-Responders [2]	9 (75.00)	6 (85.71)
		Responders	3 (25.00)	1 (14.29)
		OR (95% CI)	2.00 (0.17, 24.07)	
		RR (95% CI)	1.75 (0.22, 13.76)	
		RD % (95% CI)	10.71 (-24.95, 46.38)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	1 (14.29)
		Non-Responders [2]	8 (66.67)	6 (85.71)
		Responders	4 (33.33)	1 (14.29)
		OR (95% CI)	3.00 (0.26, 34.20)	
		RR (95% CI)	2.33 (0.32, 16.95)	
		RD % (95% CI)	19.05 (-18.15, 56.24)	
		p-value – Fisher's Exact Test	0.6027	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
Table Generation: 11SEP2023 12:13:45 PM

2MWT responders ≥ 15% improvement by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (22.22)	0 (0.00)
		Non-Responders [2]	7 (77.78)	4 (100.00)
		Responders	2 (22.22)	0 (0.00)
		OR (95% CI)	3.00 (0.12, 77.64)	
		RR (95% CI)	2.50 (0.15, 42.80)	
		RD % (95% CI)	15.00 (-22.57, 52.57)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	7 (77.78)	3 (75.00)
		Responders	2 (22.22)	1 (25.00)
		OR (95% CI)	0.86 (0.05, 13.48)	
		RR (95% CI)	0.89 (0.11, 7.20)	
		RD % (95% CI)	-2.78 (-53.16, 47.60)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
Table Generation: 11SEP2023 12:13:45 PM

4.10.2.10 2MWT responders ≥ 15% improvement by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Age Group, p-value Chi-Square[1]	0.9779	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (25.00)	0 (0.00)
		Non-Responders [2]	10 (83.33)	3 (75.00)
		Responders	2 (16.67)	1 (25.00)
		OR (95% CI)	0.60 (0.04, 9.16)	
		RR (95% CI)	0.67 (0.08, 5.54)	
		RD % (95% CI)	-8.33 (-55.72, 39.05)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	9 (75.00)	4 (100.00)
		Responders	3 (25.00)	0 (0.00)
		OR (95% CI)	3.32 (0.14, 78.81)	
		RR (95% CI)	2.69 (0.17, 43.31)	
		RD % (95% CI)	16.92 (-18.75, 52.60)	
		p-value – Fisher's Exact Test	0.5286	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
Program: t-qs-categ-sub.sas
Table Generation: 11SEP2023 12:14:09 PM

2MWT responders ≥ 15% improvement by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (14.29)
		Non-Responders [2]	6 (66.67)	7 (100.00)
		Responders	3 (33.33)	0 (0.00)
		OR (95% CI)	8.08 (0.35, 187.32)	
		RR (95% CI)	5.60 (0.34, 93.35)	
		RD % (95% CI)	28.75 (-5.24, 62.74)	
		p-value – Fisher's Exact Test	0.2125	
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	1 (14.29)
		Non-Responders [2]	6 (66.67)	5 (71.43)
		Responders	3 (33.33)	2 (28.57)
		OR (95% CI)	1.25 (0.15, 10.70)	
		RR (95% CI)	1.17 (0.26, 5.19)	
		RD % (95% CI)	4.76 (-40.72, 50.24)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
Program: t-qs-categ-sub.sas
Table Generation: 11SEP2023 12:14:09 PM

4.10.2.11 2MWT responders ≥ 15% improvement by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Region, p-value Chi-Square[1]	0.6201	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (12.50)	0 (0.00)
		Non-Responders [2]	6 (75.00)	5 (83.33)
		Responders	2 (25.00)	1 (16.67)
		OR (95% CI)	1.67 (0.11, 24.26)	
		RR (95% CI)	1.50 (0.17, 12.94)	
		RD % (95% CI)	8.33 (-33.97, 50.64)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (12.50)	0 (0.00)
		Non-Responders [2]	5 (62.50)	5 (83.33)
		Responders	3 (37.50)	1 (16.67)
		OR (95% CI)	3.00 (0.23, 39.61)	
		RR (95% CI)	2.25 (0.30, 16.63)	
		RD % (95% CI)	20.83 (-24.05, 65.72)	
		p-value – Fisher's Exact Test	0.5804	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
Table Generation: 11SEP2023 12:14:34 PM

2MWT responders ≥ 15% improvement by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (23.08)	1 (20.00)
		Non-Responders [2]	10 (76.92)	5 (100.00)
		Responders	3 (23.08)	0 (0.00)
		OR (95% CI)	3.67 (0.16, 84.51)	
		RR (95% CI)	3.00 (0.18, 49.56)	
		RD % (95% CI)	16.67 (-15.01, 48.35)	
		p-value – Fisher's Exact Test	0.5221	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (7.69)	1 (20.00)
		Non-Responders [2]	10 (76.92)	4 (80.00)
		Responders	3 (23.08)	1 (20.00)
		OR (95% CI)	1.20 (0.09, 15.26)	
		RR (95% CI)	1.15 (0.15, 8.65)	
		RD % (95% CI)	3.08 (-38.80, 44.96)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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4.10.2.12 2MWT responders ≥ 15% improvement by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.3206	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (22.22)	0 (0.00)
		Non-Responders [2]	7 (77.78)	5 (100.00)
		Responders	2 (22.22)	0 (0.00)
		OR (95% CI)	3.67 (0.15, 92.65)	
		RR (95% CI)	3.00 (0.17, 52.53)	
		RD % (95% CI)	16.67 (-18.11, 51.44)	
		p-value – Fisher's Exact Test	0.5055	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (22.22)	0 (0.00)
		Non-Responders [2]	8 (88.89)	4 (80.00)
		Responders	1 (11.11)	1 (20.00)
		OR (95% CI)	0.50 (0.02, 10.25)	
		RR (95% CI)	0.56 (0.04, 7.09)	
		RD % (95% CI)	-8.89 (-49.52, 31.74)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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2MWT responders ≥ 15% improvement by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (16.67)
		Non-Responders [2]	9 (75.00)	5 (83.33)
		Responders	3 (25.00)	1 (16.67)
		OR (95% CI)	1.67 (0.13, 20.58)	
		RR (95% CI)	1.50 (0.20, 11.54)	
		RD % (95% CI)	8.33 (-30.26, 46.93)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	1 (16.67)
		Non-Responders [2]	7 (58.33)	5 (83.33)
		Responders	5 (41.67)	1 (16.67)
		OR (95% CI)	3.57 (0.31, 40.75)	
		RR (95% CI)	2.50 (0.37, 16.89)	
		RD % (95% CI)	25.00 (-15.83, 65.83)	
		p-value – Fisher's Exact Test	0.6000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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4.10.3 Subgruppenanalysen für den Endpunkt GMFM-E

4.10.3.1 Analysen auf Basis des Full Analysis Set (inklusive Patienten mit Baseline-GMFCS ≥ IV)

4.10.3.1.1 GMFM-E by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.9644	
Male	Baseline	Absolute value	n (%)	12 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	48.17 (21.328)	43.57 (23.522)
	Week 12	Absolute value	n (%)	10 (83.33)	7 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	49.90 (22.393)	38.71 (29.398)
		Change from Baseline	n (%)	10 (83.33)	7 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	3.44 (3.308)	-4.92 (4.091)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	8.35 (5.265)	
			95% CI for LS Mean Difference [2]	-2.89, 19.60	
			p-value MMRM [2]	0.1339	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.72	
			95% CI for SMD (Hedges' g)	-0.28, 1.72	
			p-value WRS[3]	0.4827	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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1.4.3.1 GMFM-E
GMFM-E by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	11 (91.67)	7 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	50.00 (21.986)	42.43 (25.735)
		Change from Baseline	n (%)	11 (91.67)	7 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	2.94 (2.458)	-1.20 (3.087)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	4.14 (3.952)	
			95% CI for LS Mean Difference [2]	-4.28, 12.56	
			p-value MMRM [2]	0.3112	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.47	
			95% CI for SMD (Hedges' g)	-0.49, 1.43	
			p-value WRS[3]	0.7216	
Female	Baseline	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	48.56 (19.171)	51.50 (29.172)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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1.4.3.1 GMFM-E
GMFM-E by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	58.25 (9.407)	51.25 (31.042)
		Change from Baseline	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	3.60 (1.694)	-0.27 (2.505)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.87 (3.024)	
			95% CI for LS Mean Difference [2]	-2.93, 10.67	
			p-value MMRM [2]	0.2317	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.70	
			95% CI for SMD (Hedges' g)	-0.54, 1.93	
			p-value WRS[3]	0.0788	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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1.4.3.1 GMFM-E
GMFM-E by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	54.33 (21.418)	52.50 (28.160)
		Change from Baseline	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	6.00 (2.283)	0.98 (3.409)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	5.03 (4.104)	
			95% CI for LS Mean Difference [2]	-4.15, 14.20	
			p-value MMRM [2]	0.2494	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.64	
			95% CI for SMD (Hedges' g)	-0.56, 1.85	
			p-value WRS[3]	0.3483	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.3.1.2 GMFM-E by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.8708	
<10.5 years old at screening	Baseline	Absolute value	n (%)	12 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	47.33 (16.610)	42.50 (24.187)
	Week 12	Absolute value	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	51.40 (17.539)	43.75 (26.663)
		Change from Baseline	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	4.95 (1.746)	1.39 (2.887)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.56 (3.379)	
			95% CI for LS Mean Difference [2]	-3.82, 10.94	
			p-value MMRM [2]	0.3131	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.57	
			95% CI for SMD (Hedges' g)	-0.61, 1.75	
			p-value WRS[3]	0.2917	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

NOTE: Median age used as cut-off point.

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GMFM-E by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	53.55 (17.096)	46.00 (24.993)
		Change from Baseline	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	7.33 (2.315)	3.64 (3.844)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.69 (4.490)	
			95% CI for LS Mean Difference [2]	-6.07, 13.45	
			p-value MMRM [2]	0.4263	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.43	
			95% CI for SMD (Hedges' g)	-0.72, 1.59	
			p-value WRS[3]	0.6410	
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	49.67 (24.703)	48.71 (26.393)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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GMFM-E by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	8 (88.89)	7 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	56.38 (19.138)	43.00 (32.512)
		Change from Baseline	n (%)	8 (88.89)	7 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.69 (3.333)	-5.64 (3.680)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	6.32 (4.960)	
			95% CI for LS Mean Difference [2]	-4.33, 16.97	
			p-value MMRM [2]	0.2236	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.60	
			95% CI for SMD (Hedges' g)	-0.44, 1.64	
			p-value WRS[3]	0.1181	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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GMFM-E by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	50.00 (26.486)	46.14 (28.098)
		Change from Baseline	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.37 (1.937)	-2.49 (2.199)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.87 (2.928)	
			95% CI for LS Mean Difference [2]	-3.45, 9.19	
			p-value MMRM [2]	0.3453	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.45	
			95% CI for SMD (Hedges' g)	-0.55, 1.45	
			p-value WRS[3]	0.6198	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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4.10.3.1.3 GMFM-E by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.4665	
US	Baseline	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	49.75 (18.919)	48.00 (25.503)
	Week 12	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	54.00 (17.655)	49.17 (25.631)
		Change from Baseline	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	4.30 (1.592)	1.10 (1.839)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.20 (2.433)	
			95% CI for LS Mean Difference [2]	-2.14, 8.54	
			p-value MMRM [2]	0.2144	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.63	
			95% CI for SMD (Hedges' g)	-0.45, 1.72	
			p-value WRS[3]	0.1901	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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GMFM-E by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	55.38 (19.093)	50.17 (25.918)
		Change from Baseline	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	5.68 (2.180)	2.10 (2.518)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.58 (3.331)	
			95% CI for LS Mean Difference [2]	-3.71, 10.86	
			p-value MMRM [2]	0.3048	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.52	
			95% CI for SMD (Hedges' g)	-0.56, 1.60	
			p-value WRS[3]	0.5032	
Non-US	Baseline	Absolute value	n (%)	13 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	47.46 (21.239)	44.60 (26.216)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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GMFM-E by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	10 (76.92)	5 (100.00)
			Number of patients with missing data: n (%)	3 (23.08)	0 (0.00)
			Mean (SD)	53.30 (19.027)	36.20 (34.398)
		Change from Baseline	n (%)	10 (76.92)	5 (100.00)
			Number of patients with missing data: n (%)	3 (23.08)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	2.56 (3.161)	-8.41 (4.715)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	10.97 (5.671)	
			95% CI for LS Mean Difference [2]	-1.33, 23.28	
			p-value MMRM [2]	0.0760	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.98	
			95% CI for SMD (Hedges' g)	-0.16, 2.11	
			p-value WRS[3]	0.0892	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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GMFM-E by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	12 (92.31)	5 (100.00)
			Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
			Mean (SD)	49.67 (23.137)	41.20 (27.535)
		Change from Baseline	n (%)	12 (92.31)	5 (100.00)
			Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	3.25 (2.394)	-3.41 (3.717)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	6.66 (4.415)	
			95% CI for LS Mean Difference [2]	-2.81, 16.13	
			p-value MMRM [2]	0.1537	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.73	
			95% CI for SMD (Hedges' g)	-0.34, 1.81	
			p-value WRS[3]	0.3379	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.3.1.4 GMFM-E by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.5018	
I	Baseline	Absolute value	n (%)	9 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	60.78 (9.985)	66.20 (6.686)
	Week 12	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	62.63 (9.591)	66.60 (6.693)
		Change from Baseline	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	1.42 (0.987)	0.93 (1.264)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.49 (1.643)	
			95% CI for LS Mean Difference [2]	-3.18, 4.17	
			p-value MMRM [2]	0.7696	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.15	
			95% CI for SMD (Hedges' g)	-0.96, 1.27	
			p-value WRS[3]	0.6799	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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GMFM-E by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	63.75 (8.746)	66.40 (4.879)
		Change from Baseline	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	2.55 (1.089)	0.73 (1.391)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.82 (1.802)	
			95% CI for LS Mean Difference [2]	-2.25, 5.89	
			p-value MMRM [2]	0.3388	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.51	
			95% CI for SMD (Hedges' g)	-0.63, 1.65	
			p-value WRS[3]	0.3753	
≥ II	Baseline	Absolute value	n (%)	12 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	39.00 (20.688)	30.00 (21.354)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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GMFM-E by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	10 (83.33)	6 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	46.40 (20.079)	23.83 (25.725)
		Change from Baseline	n (%)	10 (83.33)	6 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	4.08 (3.277)	-5.87 (4.546)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	9.96 (5.642)	
			95% CI for LS Mean Difference [2]	-2.06, 21.97	
			p-value MMRM [2]	0.0978	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.86	
			95% CI for SMD (Hedges' g)	-0.20, 1.92	
			p-value WRS[3]	0.1016	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
Program: t-qs-cont-sub.sas
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GMFM-E by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	12 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	44.08 (23.750)	29.17 (23.387)
		Change from Baseline	n (%)	12 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	4.99 (2.720)	-0.54 (3.916)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	5.53 (4.811)	
			95% CI for LS Mean Difference [2]	-4.72, 15.79	
			p-value MMRM [2]	0.2681	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.54	
			95% CI for SMD (Hedges' g)	-0.46, 1.53	
			p-value WRS[3]	0.4786	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.3.1.5 GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Gender, p-value Chi-Square[1]	0.9730	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	9 (75.00)	5 (71.43)
		Responders	3 (25.00)	2 (28.57)
		OR (95% CI)	0.83 (0.10, 6.78)	
		RR (95% CI)	0.88 (0.19, 4.03)	
		RD % (95% CI)	-3.57 (-45.05, 37.90)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [2]	8 (66.67)	5 (71.43)
		Responders	4 (33.33)	2 (28.57)
		OR (95% CI)	1.25 (0.16, 9.54)	
		RR (95% CI)	1.17 (0.28, 4.82)	
		RD % (95% CI)	4.76 (-38.03, 47.56)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	5 (55.56)	4 (100.00)
		Responders	4 (44.44)	0 (0.00)
		OR (95% CI)	7.36 (0.31, 176.41)	
		RR (95% CI)	4.50 (0.30, 68.13)	
		RD % (95% CI)	35.00 (-5.52, 75.52)	
		p-value – Fisher's Exact Test	0.2280	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	4 (44.44)	4 (100.00)
		Responders	5 (55.56)	0 (0.00)
		OR (95% CI)	11.00 (0.46, 263.53)	
		RR (95% CI)	5.50 (0.37, 80.92)	
		RD % (95% CI)	45.00 (4.48, 85.52)	
		p-value – Fisher's Exact Test	0.1049	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.3.1.6 GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Age Group, p-value Chi-Square[1]	0.9686	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	6 (50.00)	2 (50.00)
		Responders	6 (50.00)	2 (50.00)
		OR (95% CI)	1.00 (0.10, 9.61)	
		RR (95% CI)	1.00 (0.32, 3.10)	
		RD % (95% CI)	0.00 (-56.58, 56.58)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [2]	5 (41.67)	2 (50.00)
		Responders	7 (58.33)	2 (50.00)
		OR (95% CI)	1.40 (0.14, 13.57)	
		RR (95% CI)	1.17 (0.39, 3.47)	
		RD % (95% CI)	8.33 (-48.05, 64.72)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	8 (88.89)	7 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	2.65 (0.09, 75.29)	
		RR (95% CI)	2.40 (0.11, 51.32)	
		RD % (95% CI)	8.75 (-19.02, 36.52)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	7 (77.78)	7 (100.00)
		Responders	2 (22.22)	0 (0.00)
		OR (95% CI)	5.00 (0.20, 122.74)	
		RR (95% CI)	4.00 (0.22, 72.01)	
		RD % (95% CI)	18.75 (-12.90, 50.40)	
		p-value – Fisher's Exact Test	0.4750	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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4.10.3.1.7 GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Region, p-value Chi-Square[1]	0.9725	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	4 (50.00)	4 (66.67)
		Responders	4 (50.00)	2 (33.33)
		OR (95% CI)	2.00 (0.22, 17.89)	
		RR (95% CI)	1.50 (0.40, 5.65)	
		RD % (95% CI)	16.67 (-34.55, 67.88)	
		p-value – Fisher's Exact Test	0.6270	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	4 (50.00)	4 (66.67)
		Responders	4 (50.00)	2 (33.33)
		OR (95% CI)	2.00 (0.22, 17.89)	
		RR (95% CI)	1.50 (0.40, 5.65)	
		RD % (95% CI)	16.67 (-34.55, 67.88)	
		p-value – Fisher's Exact Test	0.6270	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (23.08)	0 (0.00)
		Non-Responders [2]	10 (76.92)	5 (100.00)
		Responders	3 (23.08)	0 (0.00)
		OR (95% CI)	3.67 (0.16, 84.51)	
		RR (95% CI)	3.00 (0.18, 49.56)	
		RD % (95% CI)	16.67 (-15.01, 48.35)	
		p-value – Fisher's Exact Test	0.5221	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (7.69)	0 (0.00)
		Non-Responders [2]	8 (61.54)	5 (100.00)
		Responders	5 (38.46)	0 (0.00)
		OR (95% CI)	7.12 (0.32, 156.01)	
		RR (95% CI)	4.71 (0.31, 72.47)	
		RD % (95% CI)	30.95 (-2.86, 64.77)	
		p-value – Fisher's Exact Test	0.2489	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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4.10.3.1.8 GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.9730	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	6 (66.67)	5 (100.00)
		Responders	3 (33.33)	0 (0.00)
		OR (95% CI)	5.92 (0.25, 141.48)	
		RR (95% CI)	4.20 (0.26, 68.04)	
		RD % (95% CI)	26.67 (-10.25, 63.59)	
		p-value – Fisher's Exact Test	0.2582	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	6 (66.67)	5 (100.00)
		Responders	3 (33.33)	0 (0.00)
		OR (95% CI)	5.92 (0.25, 141.48)	
		RR (95% CI)	4.20 (0.26, 68.04)	
		RD % (95% CI)	26.67 (-10.25, 63.59)	
		p-value – Fisher's Exact Test	0.2582	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	8 (66.67)	4 (66.67)
		Responders	4 (33.33)	2 (33.33)
		OR (95% CI)	1.00 (0.13, 8.00)	
		RR (95% CI)	1.00 (0.25, 4.00)	
		RD % (95% CI)	0.00 (-46.20, 46.20)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	6 (50.00)	4 (66.67)
		Responders	6 (50.00)	2 (33.33)
		OR (95% CI)	2.00 (0.26, 15.38)	
		RR (95% CI)	1.50 (0.42, 5.32)	
		RD % (95% CI)	16.67 (-30.48, 63.82)	
		p-value – Fisher's Exact Test	0.6380	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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4.10.3.1.9 GMFM-E responders ≥ 10,8 by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Gender, p-value Chi-Square[1]	0.9994	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	11 (91.67)	7 (100.00)
		Responders	1 (8.33)	0 (0.00)
		OR (95% CI)	1.96 (0.07, 54.67)	
		RR (95% CI)	1.85 (0.09, 40.05)	
		RD % (95% CI)	5.29 (-18.86, 29.43)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [2]	10 (83.33)	7 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	3.57 (0.15, 85.68)	
		RR (95% CI)	3.08 (0.17, 56.25)	
		RD % (95% CI)	12.98 (-14.23, 40.19)	
		p-value – Fisher's Exact Test	0.5088	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
Table Generation: 11SEP2023 12:15:14 PM

GMFM-E responders ≥ 10,8 by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	8 (88.89)	4 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	1.59 (0.05, 47.52)	
		RR (95% CI)	1.50 (0.07, 30.59)	
		RD % (95% CI)	5.00 (-29.37, 39.37)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	7 (77.78)	4 (100.00)
		Responders	2 (22.22)	0 (0.00)
		OR (95% CI)	3.00 (0.12, 77.64)	
		RR (95% CI)	2.50 (0.15, 42.80)	
		RD % (95% CI)	15.00 (-22.57, 52.57)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
Table Generation: 11SEP2023 12:15:14 PM

4.10.3.1.10 GMFM-E responders ≥ 10,8 by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Age Group, p-value Chi-Square[1]	0.9705	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	10 (83.33)	4 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	2.14 (0.08, 54.22)	
		RR (95% CI)	1.92 (0.11, 33.44)	
		RD % (95% CI)	9.23 (-24.69, 43.15)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [2]	8 (66.67)	4 (100.00)
		Responders	4 (33.33)	0 (0.00)
		OR (95% CI)	4.76 (0.21, 109.78)	
		RR (95% CI)	3.46 (0.22, 53.27)	
		RD % (95% CI)	24.62 (-12.27, 61.50)	
		p-value – Fisher's Exact Test	0.5165	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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GMFM-E responders ≥ 10,8 by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	9 (100.00)	7 (100.00)
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	9 (100.00)	7 (100.00)

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
Program: t-qs-categ-sub.sas
Table Generation: 11SEP2023 12:15:20 PM

4.10.3.1.11 GMFM-E responders ≥ 10,8 by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Region, p-value Chi-Square[1]	0.9989	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	7 (87.50)	6 (100.00)
		Responders	1 (12.50)	0 (0.00)
		OR (95% CI)	2.60 (0.09, 75.49)	
		RR (95% CI)	2.33 (0.11, 48.99)	
		RD % (95% CI)	9.52 (-21.41, 40.46)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	6 (75.00)	6 (100.00)
		Responders	2 (25.00)	0 (0.00)
		OR (95% CI)	5.00 (0.20, 125.78)	
		RR (95% CI)	3.89 (0.22, 68.67)	
		RD % (95% CI)	20.63 (-14.30, 55.57)	
		p-value – Fisher's Exact Test	0.4725	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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GMFM-E responders ≥ 10,8 by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (23.08)	0 (0.00)
		Non-Responders [2]	12 (92.31)	5 (100.00)
		Responders	1 (7.69)	0 (0.00)
		OR (95% CI)	1.32 (0.05, 37.78)	
		RR (95% CI)	1.29 (0.06, 27.27)	
		RD % (95% CI)	2.38 (-25.03, 29.80)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (7.69)	0 (0.00)
		Non-Responders [2]	11 (84.62)	5 (100.00)
		Responders	2 (15.38)	0 (0.00)
		OR (95% CI)	2.39 (0.10, 58.77)	
		RR (95% CI)	2.14 (0.12, 38.24)	
		RD % (95% CI)	9.52 (-20.34, 39.38)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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4.10.3.1.12 GMFM-E responders ≥ 10,8 by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.9982	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	9 (100.00)	5 (100.00)
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	8 (88.89)	5 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	1.94 (0.07, 56.76)	
		RR (95% CI)	1.80 (0.09, 37.49)	
		RD % (95% CI)	6.67 (-24.62, 37.95)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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GMFM-E responders ≥ 10,8 by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	10 (83.33)	6 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	3.10 (0.13, 75.18)	
		RR (95% CI)	2.69 (0.15, 48.64)	
		RD % (95% CI)	12.09 (-16.60, 40.78)	
		p-value – Fisher's Exact Test	0.5294	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	9 (75.00)	6 (100.00)
		Responders	3 (25.00)	0 (0.00)
		OR (95% CI)	4.79 (0.21, 109.19)	
		RR (95% CI)	3.77 (0.23, 63.05)	
		RD % (95% CI)	19.78 (-10.97, 50.53)	
		p-value – Fisher's Exact Test	0.5147	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
Table Generation: 11SEP2023 12:15:31 PM

4.10.3.1.13 GMFM-E - excluding subject with data entry error by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.9461	
Male	Baseline	Absolute value	n (%)	12 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	48.17 (21.328)	43.57 (23.522)
	Week 12	Absolute value	n (%)	10 (83.33)	7 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	49.90 (22.393)	38.71 (29.398)
		Change from Baseline	n (%)	10 (83.33)	7 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	3.44 (3.308)	-4.92 (4.091)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	8.35 (5.265)	
			95% CI for LS Mean Difference [2]	-2.89, 19.60	
			p-value MMRM [2]	0.1339	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.72	
			95% CI for SMD (Hedges' g)	-0.28, 1.72	
			p-value WRS[3]	0.4827	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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GMFM-E - excluding subject with data entry error by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	11 (91.67)	7 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	50.00 (21.986)	42.43 (25.735)
		Change from Baseline	n (%)	11 (91.67)	7 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	2.94 (2.458)	-1.20 (3.087)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	4.14 (3.952)	
			95% CI for LS Mean Difference [2]	-4.28, 12.56	
			p-value MMRM [2]	0.3112	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.47	
			95% CI for SMD (Hedges' g)	-0.49, 1.43	
			p-value WRS[3]	0.7216	
Female	Baseline	Absolute value	n (%)	9 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			Mean (SD)	48.56 (19.171)	65.67 (8.505)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
Program: t-qs-cont-sub.sas
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GMFM-E - excluding subject with data entry error by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	8 (88.89)	3 (75.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (25.00)
			Mean (SD)	58.25 (9.407)	66.33 (8.963)
		Change from Baseline	n (%)	8 (88.89)	3 (75.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	3.76 (1.831)	0.08 (3.264)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.68 (3.922)	
			95% CI for LS Mean Difference [2]	-5.23, 12.58	
			p-value MMRM [2]	0.3734	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.60	
			95% CI for SMD (Hedges' g)	-0.76, 1.95	
			p-value WRS[3]	0.2182	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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GMFM-E - excluding subject with data entry error by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	9 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			Mean (SD)	54.33 (21.418)	66.33 (6.429)
		Change from Baseline	n (%)	9 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	6.13 (2.446)	0.08 (4.227)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	6.05 (5.081)	
			95% CI for LS Mean Difference [2]	-5.28, 17.37	
			p-value MMRM [2]	0.2616	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.72	
			95% CI for SMD (Hedges' g)	-0.62, 2.07	
			p-value WRS[3]	0.3455	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
Program: t-qs-cont-sub.sas
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4.10.3.1.14 GMFM-E - excluding subject with data entry error by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.9410	
<10.5 years old at screening	Baseline	Absolute value	n (%)	12 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			Mean (SD)	47.33 (16.610)	53.67 (11.372)
	Week 12	Absolute value	n (%)	10 (83.33)	3 (75.00)
			Number of patients with missing data: n (%)	2 (16.67)	1 (25.00)
			Mean (SD)	51.40 (17.539)	56.33 (10.786)
		Change from Baseline	n (%)	10 (83.33)	3 (75.00)
			Number of patients with missing data: n (%)	2 (16.67)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	4.92 (1.697)	2.86 (3.257)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.05 (3.690)	
			95% CI for LS Mean Difference [2]	-6.02, 10.13	
			p-value MMRM [2]	0.5885	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.34	
			95% CI for SMD (Hedges' g)	-0.96, 1.64	
			p-value WRS[3]	0.6049	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

NOTE: Median age used as cut-off point.

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GMFM-E - excluding subject with data entry error by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	11 (91.67)	3 (75.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (25.00)
			Mean (SD)	53.55 (17.096)	57.67 (10.970)
		Change from Baseline	n (%)	11 (91.67)	3 (75.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	7.29 (2.315)	4.20 (4.445)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.09 (5.026)	
			95% CI for LS Mean Difference [2]	-7.86, 14.05	
			p-value MMRM [2]	0.5496	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.36	
			95% CI for SMD (Hedges' g)	-0.92, 1.65	
			p-value WRS[3]	0.7445	
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	49.67 (24.703)	48.71 (26.393)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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GMFM-E - excluding subject with data entry error by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	8 (88.89)	7 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	56.38 (19.138)	43.00 (32.512)
		Change from Baseline	n (%)	8 (88.89)	7 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.69 (3.333)	-5.64 (3.680)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	6.32 (4.960)	
			95% CI for LS Mean Difference [2]	-4.33, 16.97	
			p-value MMRM [2]	0.2236	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.60	
			95% CI for SMD (Hedges' g)	-0.44, 1.64	
			p-value WRS[3]	0.1181	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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GMFM-E - excluding subject with data entry error by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	50.00 (26.486)	46.14 (28.098)
		Change from Baseline	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.37 (1.937)	-2.49 (2.199)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.87 (2.928)	
			95% CI for LS Mean Difference [2]	-3.45, 9.19	
			p-value MMRM [2]	0.3453	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.45	
			95% CI for SMD (Hedges' g)	-0.55, 1.45	
			p-value WRS[3]	0.6198	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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4.10.3.1.15 GMFM-E - excluding subject with data entry error by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.3483	
US	Baseline	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	49.75 (18.919)	48.00 (25.503)
	Week 12	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	54.00 (17.655)	49.17 (25.631)
		Change from Baseline	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	4.30 (1.592)	1.10 (1.839)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.20 (2.433)	
			95% CI for LS Mean Difference [2]	-2.14, 8.54	
			p-value MMRM [2]	0.2144	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.63	
			95% CI for SMD (Hedges' g)	-0.45, 1.72	
			p-value WRS[3]	0.1901	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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GMFM-E - excluding subject with data entry error by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	55.38 (19.093)	50.17 (25.918)
		Change from Baseline	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	5.68 (2.180)	2.10 (2.518)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.58 (3.331)	
			95% CI for LS Mean Difference [2]	-3.71, 10.86	
			p-value MMRM [2]	0.3048	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.52	
			95% CI for SMD (Hedges' g)	-0.56, 1.60	
			p-value WRS[3]	0.5032	
Non-US	Baseline	Absolute value	n (%)	13 (100.00)	4 (80.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (20.00)
			Mean (SD)	47.46 (21.239)	53.50 (19.706)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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GMFM-E - excluding subject with data entry error by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	10 (76.92)	4 (80.00)
			Number of patients with missing data: n (%)	3 (23.08)	1 (20.00)
			Mean (SD)	53.30 (19.027)	43.75 (34.606)
		Change from Baseline	n (%)	10 (76.92)	4 (80.00)
			Number of patients with missing data: n (%)	3 (23.08)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	2.67 (3.214)	-9.87 (5.312)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	12.55 (6.234)	
			95% CI for LS Mean Difference [2]	-1.15, 26.24	
			p-value MMRM [2]	0.0689	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.09	
			95% CI for SMD (Hedges' g)	-0.15, 2.33	
			p-value WRS[3]	0.2328	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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GMFM-E - excluding subject with data entry error by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	12 (92.31)	4 (80.00)
			Number of patients with missing data: n (%)	1 (7.69)	1 (20.00)
			Mean (SD)	49.67 (23.137)	48.75 (25.118)
		Change from Baseline	n (%)	12 (92.31)	4 (80.00)
			Number of patients with missing data: n (%)	1 (7.69)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	3.38 (2.458)	-4.87 (4.218)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	8.25 (4.914)	
			95% CI for LS Mean Difference [2]	-2.37, 18.87	
			p-value MMRM [2]	0.1170	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.88	
			95% CI for SMD (Hedges' g)	-0.30, 2.06	
			p-value WRS[3]	0.2478	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.3.1.16 GMFM-E - excluding subject with data entry error by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.4681	
I	Baseline	Absolute value	n (%)	9 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	60.78 (9.985)	66.20 (6.686)
	Week 12	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	62.63 (9.591)	66.60 (6.693)
		Change from Baseline	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	1.42 (0.987)	0.93 (1.264)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.49 (1.643)	
			95% CI for LS Mean Difference [2]	-3.18, 4.17	
			p-value MMRM [2]	0.7696	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.15	
			95% CI for SMD (Hedges' g)	-0.96, 1.27	
			p-value WRS[3]	0.6799	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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GMFM-E - excluding subject with data entry error by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	63.75 (8.746)	66.40 (4.879)
		Change from Baseline	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	2.55 (1.089)	0.73 (1.391)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.82 (1.802)	
			95% CI for LS Mean Difference [2]	-2.25, 5.89	
			p-value MMRM [2]	0.3388	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.51	
			95% CI for SMD (Hedges' g)	-0.63, 1.65	
			p-value WRS[3]	0.3753	
≥ II	Baseline	Absolute value	n (%)	12 (100.00)	5 (83.33)
			Number of patients with missing data: n (%)	0 (0.00)	1 (16.67)
			Mean (SD)	39.00 (20.688)	34.20 (20.921)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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GMFM-E - excluding subject with data entry error by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	10 (83.33)	5 (83.33)
			Number of patients with missing data: n (%)	2 (16.67)	1 (16.67)
			Mean (SD)	46.40 (20.079)	27.40 (27.052)
		Change from Baseline	n (%)	10 (83.33)	5 (83.33)
			Number of patients with missing data: n (%)	2 (16.67)	1 (16.67)
			LS Mean Change from Baseline (SE) [2]	4.15 (3.372)	-6.55 (5.086)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	10.70 (6.107)	
			95% CI for LS Mean Difference [2]	-2.42, 23.82	
			p-value MMRM [2]	0.1021	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.90	
			95% CI for SMD (Hedges' g)	-0.23, 2.03	
			p-value WRS[3]	0.2165	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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GMFM-E - excluding subject with data entry error by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	12 (100.00)	5 (83.33)
			Number of patients with missing data: n (%)	0 (0.00)	1 (16.67)
			Mean (SD)	44.08 (23.750)	32.80 (24.181)
		Change from Baseline	n (%)	12 (100.00)	5 (83.33)
			Number of patients with missing data: n (%)	0 (0.00)	1 (16.67)
			LS Mean Change from Baseline (SE) [2]	5.06 (2.784)	-1.15 (4.349)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	6.21 (5.169)	
			95% CI for LS Mean Difference [2]	-4.88, 17.29	
			p-value MMRM [2]	0.2497	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.59	
			95% CI for SMD (Hedges' g)	-0.48, 1.65	
			p-value WRS[3]	0.4263	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.3.1.17 GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) - excluding subject with data entry error by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Gender, p-value Chi-Square[1]	0.9730	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	9 (75.00)	5 (71.43)
		Responders	3 (25.00)	2 (28.57)
		OR (95% CI)	0.83 (0.10, 6.78)	
		RR (95% CI)	0.88 (0.19, 4.03)	
		RD % (95% CI)	-3.57 (-45.05, 37.90)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [2]	8 (66.67)	5 (71.43)
		Responders	4 (33.33)	2 (28.57)
		OR (95% CI)	1.25 (0.16, 9.54)	
		RR (95% CI)	1.17 (0.28, 4.82)	
		RD % (95% CI)	4.76 (-38.03, 47.56)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) - excluding subject with data entry error by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (25.00)
		Non-Responders [2]	5 (55.56)	4 (100.00)
		Responders	4 (44.44)	0 (0.00)
		OR (95% CI)	7.36 (0.31, 176.41)	
		RR (95% CI)	4.50 (0.30, 68.13)	
		RD % (95% CI)	35.00 (-5.52, 75.52)	
		p-value – Fisher's Exact Test	0.2280	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	1 (25.00)
		Non-Responders [2]	4 (44.44)	4 (100.00)
		Responders	5 (55.56)	0 (0.00)
		OR (95% CI)	11.00 (0.46, 263.53)	
		RR (95% CI)	5.50 (0.37, 80.92)	
		RD % (95% CI)	45.00 (4.48, 85.52)	
		p-value – Fisher's Exact Test	0.1049	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.3.1.18 GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) - excluding subject with data entry error by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Age Group, p-value Chi-Square[1]	0.9686	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (25.00)
		Non-Responders [2]	6 (50.00)	2 (50.00)
		Responders	6 (50.00)	2 (50.00)
		OR (95% CI)	1.00 (0.10, 9.61)	
		RR (95% CI)	1.00 (0.32, 3.10)	
		RD % (95% CI)	0.00 (-56.58, 56.58)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	1 (25.00)
		Non-Responders [2]	5 (41.67)	2 (50.00)
		Responders	7 (58.33)	2 (50.00)
		OR (95% CI)	1.40 (0.14, 13.57)	
		RR (95% CI)	1.17 (0.39, 3.47)	
		RD % (95% CI)	8.33 (-48.05, 64.72)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) - excluding subject with data entry error by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	8 (88.89)	7 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	2.65 (0.09, 75.29)	
		RR (95% CI)	2.40 (0.11, 51.32)	
		RD % (95% CI)	8.75 (-19.02, 36.52)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	7 (77.78)	7 (100.00)
		Responders	2 (22.22)	0 (0.00)
		OR (95% CI)	5.00 (0.20, 122.74)	
		RR (95% CI)	4.00 (0.22, 72.01)	
		RD % (95% CI)	18.75 (-12.90, 50.40)	
		p-value – Fisher's Exact Test	0.4750	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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4.10.3.1.19 GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) - excluding subject with data entry error by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Region, p-value Chi-Square[1]	0.9725	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	4 (50.00)	4 (66.67)
		Responders	4 (50.00)	2 (33.33)
		OR (95% CI)	2.00 (0.22, 17.89)	
		RR (95% CI)	1.50 (0.40, 5.65)	
		RD % (95% CI)	16.67 (-34.55, 67.88)	
		p-value – Fisher's Exact Test	0.6270	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	4 (50.00)	4 (66.67)
		Responders	4 (50.00)	2 (33.33)
		OR (95% CI)	2.00 (0.22, 17.89)	
		RR (95% CI)	1.50 (0.40, 5.65)	
		RD % (95% CI)	16.67 (-34.55, 67.88)	
		p-value – Fisher's Exact Test	0.6270	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) - excluding subject with data entry error by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (23.08)	1 (20.00)
		Non-Responders [2]	10 (76.92)	5 (100.00)
		Responders	3 (23.08)	0 (0.00)
		OR (95% CI)	3.67 (0.16, 84.51)	
		RR (95% CI)	3.00 (0.18, 49.56)	
		RD % (95% CI)	16.67 (-15.01, 48.35)	
		p-value – Fisher's Exact Test	0.5221	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (7.69)	1 (20.00)
		Non-Responders [2]	8 (61.54)	5 (100.00)
		Responders	5 (38.46)	0 (0.00)
		OR (95% CI)	7.12 (0.32, 156.01)	
		RR (95% CI)	4.71 (0.31, 72.47)	
		RD % (95% CI)	30.95 (-2.86, 64.77)	
		p-value – Fisher's Exact Test	0.2489	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.3.1.20 GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) - excluding subject with data entry error by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.9730	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	6 (66.67)	5 (100.00)
		Responders	3 (33.33)	0 (0.00)
		OR (95% CI)	5.92 (0.25, 141.48)	
		RR (95% CI)	4.20 (0.26, 68.04)	
		RD % (95% CI)	26.67 (-10.25, 63.59)	
		p-value – Fisher's Exact Test	0.2582	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	6 (66.67)	5 (100.00)
		Responders	3 (33.33)	0 (0.00)
		OR (95% CI)	5.92 (0.25, 141.48)	
		RR (95% CI)	4.20 (0.26, 68.04)	
		RD % (95% CI)	26.67 (-10.25, 63.59)	
		p-value – Fisher's Exact Test	0.2582	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) - excluding subject with data entry error by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (16.67)
		Non-Responders [2]	8 (66.67)	4 (66.67)
		Responders	4 (33.33)	2 (33.33)
		OR (95% CI)	1.00 (0.13, 8.00)	
		RR (95% CI)	1.00 (0.25, 4.00)	
		RD % (95% CI)	0.00 (-46.20, 46.20)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	1 (16.67)
		Non-Responders [2]	6 (50.00)	4 (66.67)
		Responders	6 (50.00)	2 (33.33)
		OR (95% CI)	2.00 (0.26, 15.38)	
		RR (95% CI)	1.50 (0.42, 5.32)	
		RD % (95% CI)	16.67 (-30.48, 63.82)	
		p-value – Fisher's Exact Test	0.6380	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.3.1.21 GMFM-E responders ≥ 10,8 - excluding subject with data entry error by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Gender, p-value Chi-Square[1]	0.9994	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	11 (91.67)	7 (100.00)
		Responders	1 (8.33)	0 (0.00)
		OR (95% CI)	1.96 (0.07, 54.67)	
		RR (95% CI)	1.85 (0.09, 40.05)	
		RD % (95% CI)	5.29 (-18.86, 29.43)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [2]	10 (83.33)	7 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	3.57 (0.15, 85.68)	
		RR (95% CI)	3.08 (0.17, 56.25)	
		RD % (95% CI)	12.98 (-14.23, 40.19)	
		p-value – Fisher's Exact Test	0.5088	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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GMFM-E responders ≥ 10,8 - excluding subject with data entry error by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (25.00)
		Non-Responders [2]	8 (88.89)	4 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	1.59 (0.05, 47.52)	
		RR (95% CI)	1.50 (0.07, 30.59)	
		RD % (95% CI)	5.00 (-29.37, 39.37)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	1 (25.00)
		Non-Responders [2]	7 (77.78)	4 (100.00)
		Responders	2 (22.22)	0 (0.00)
		OR (95% CI)	3.00 (0.12, 77.64)	
		RR (95% CI)	2.50 (0.15, 42.80)	
		RD % (95% CI)	15.00 (-22.57, 52.57)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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4.10.3.1.22 GMFM-E responders ≥ 10,8 - excluding subject with data entry error by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Age Group, p-value Chi-Square[1]	0.9705	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (25.00)
		Non-Responders [2]	10 (83.33)	4 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	2.14 (0.08, 54.22)	
		RR (95% CI)	1.92 (0.11, 33.44)	
		RD % (95% CI)	9.23 (-24.69, 43.15)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	1 (25.00)
		Non-Responders [2]	8 (66.67)	4 (100.00)
		Responders	4 (33.33)	0 (0.00)
		OR (95% CI)	4.76 (0.21, 109.78)	
		RR (95% CI)	3.46 (0.22, 53.27)	
		RD % (95% CI)	24.62 (-12.27, 61.50)	
		p-value – Fisher's Exact Test	0.5165	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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GMFM-E responders ≥ 10,8 - excluding subject with data entry error by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	9 (100.00)	7 (100.00)
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	9 (100.00)	7 (100.00)

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
Program: t-qs-categ-sub.sas
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4.10.3.1.23 GMFM-E responders ≥ 10,8 - excluding subject with data entry error by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Region, p-value Chi-Square[1]	0.9989	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	7 (87.50)	6 (100.00)
		Responders	1 (12.50)	0 (0.00)
		OR (95% CI)	2.60 (0.09, 75.49)	
		RR (95% CI)	2.33 (0.11, 48.99)	
		RD % (95% CI)	9.52 (-21.41, 40.46)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	6 (75.00)	6 (100.00)
		Responders	2 (25.00)	0 (0.00)
		OR (95% CI)	5.00 (0.20, 125.78)	
		RR (95% CI)	3.89 (0.22, 68.67)	
		RD % (95% CI)	20.63 (-14.30, 55.57)	
		p-value – Fisher's Exact Test	0.4725	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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GMFM-E responders ≥ 10,8 - excluding subject with data entry error by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (23.08)	1 (20.00)
		Non-Responders [2]	12 (92.31)	5 (100.00)
		Responders	1 (7.69)	0 (0.00)
		OR (95% CI)	1.32 (0.05, 37.78)	
		RR (95% CI)	1.29 (0.06, 27.27)	
		RD % (95% CI)	2.38 (-25.03, 29.80)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (7.69)	1 (20.00)
		Non-Responders [2]	11 (84.62)	5 (100.00)
		Responders	2 (15.38)	0 (0.00)
		OR (95% CI)	2.39 (0.10, 58.77)	
		RR (95% CI)	2.14 (0.12, 38.24)	
		RD % (95% CI)	9.52 (-20.34, 39.38)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.3.1.24 GMFM-E responders ≥ 10,8 - excluding subject with data entry error by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.9982	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	9 (100.00)	5 (100.00)
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	8 (88.89)	5 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	1.94 (0.07, 56.76)	
		RR (95% CI)	1.80 (0.09, 37.49)	
		RD % (95% CI)	6.67 (-24.62, 37.95)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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GMFM-E responders ≥ 10,8 - excluding subject with data entry error by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (16.67)
		Non-Responders [2]	10 (83.33)	6 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	3.10 (0.13, 75.18)	
		RR (95% CI)	2.69 (0.15, 48.64)	
		RD % (95% CI)	12.09 (-16.60, 40.78)	
		p-value – Fisher's Exact Test	0.5294	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	1 (16.67)
		Non-Responders [2]	9 (75.00)	6 (100.00)
		Responders	3 (25.00)	0 (0.00)
		OR (95% CI)	4.79 (0.21, 109.19)	
		RR (95% CI)	3.77 (0.23, 63.05)	
		RD % (95% CI)	19.78 (-10.97, 50.53)	
		p-value – Fisher's Exact Test	0.5147	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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4.10.3.2 Analysen unter Ausschluss von Patienten mit Baseline-GMFCS ≥ IV

4.10.3.2.1 GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) by gender (patients with baseline GMFCS ≥ IV are excluded)

Gender	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
All	Interaction test at Week 24	Treatment*Gender, p-value Chi-Square[1]	0.9753	
Male	Week 12	n (%)	10 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (20.00)	0 (0.00)
		Non-Responders [2]	7 (70.00)	4 (66.67)
		Responders	3 (30.00)	2 (33.33)
		OR (95% CI)	0.86 (0.10, 7.51)	
		RR (95% CI)	0.90 (0.21, 3.94)	
		RD % (95% CI)	-3.33 (-50.55, 43.88)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	10 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (10.00)	0 (0.00)
		Non-Responders [2]	6 (60.00)	4 (66.67)
		Responders	4 (40.00)	2 (33.33)
		OR (95% CI)	1.33 (0.16, 11.07)	
		RR (95% CI)	1.20 (0.31, 4.69)	
		RD % (95% CI)	6.67 (-41.76, 55.09)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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1.4.3.2 Sensitivity analyses for GMFM-E
GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) by gender (patients with baseline GMFCS ≥ IV are excluded)

Gender	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
Female	Week 12	n (%)	8 (100.00)	3 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	4 (50.00)	3 (100.00)
		Responders	4 (50.00)	0 (0.00)
		OR (95% CI)	7.00 (0.27, 178.47)	
		RR (95% CI)	4.00 (0.28, 57.98)	
		RD % (95% CI)	37.50 (-8.52, 83.52)	
		p-value – Fisher's Exact Test	0.2364	
	Week 24	n (%)	8 (100.00)	3 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	3 (37.50)	3 (100.00)
		Responders	5 (62.50)	0 (0.00)
		OR (95% CI)	11.00 (0.43, 284.30)	
		RR (95% CI)	4.89 (0.35, 68.83)	
		RD % (95% CI)	48.61 (3.17, 94.05)	
		p-value – Fisher's Exact Test	0.1818	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.3.2.2 GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) by age group (patients with baseline GMFCS ≥ IV are excluded)

Age Group	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
All	Interaction test at Week 24	Treatment*Age Group, p-value Chi-Square[1]	0.9677	
<10.5 years old at screening	Week 12	n (%)	11 (100.00)	3 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (18.18)	0 (0.00)
		Non-Responders [2]	5 (45.45)	1 (33.33)
		Responders	6 (54.55)	2 (66.67)
		OR (95% CI)	0.60 (0.04, 8.73)	
		RR (95% CI)	0.82 (0.31, 2.15)	
		RD % (95% CI)	-12.12 (-73.04, 48.80)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	11 (100.00)	3 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (9.09)	0 (0.00)
		Non-Responders [2]	4 (36.36)	1 (33.33)
		Responders	7 (63.64)	2 (66.67)
		OR (95% CI)	0.88 (0.06, 12.97)	
		RR (95% CI)	0.95 (0.38, 2.39)	
		RD % (95% CI)	-3.03 (-63.48, 57.42)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) by age group (patients with baseline GMFCS ≥ IV are excluded)

Age Group	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	7 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	6 (85.71)	6 (100.00)
		Responders	1 (14.29)	0 (0.00)
		OR (95% CI)	3.00 (0.10, 88.13)	
		RR (95% CI)	2.63 (0.13, 54.64)	
		RD % (95% CI)	11.61 (-21.49, 44.71)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	7 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	5 (71.43)	6 (100.00)
		Responders	2 (28.57)	0 (0.00)
		OR (95% CI)	5.91 (0.23, 151.15)	
		RR (95% CI)	4.38 (0.25, 76.54)	
		RD % (95% CI)	24.11 (-13.25, 61.47)	
		p-value – Fisher's Exact Test	0.4615	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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4.10.3.2.3 GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) by region (patients with baseline GMFCS ≥ IV are excluded)

Region	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
All	Interaction test at Week 24	Treatment*Region, p-value Chi-Square[1]	0.9738	
US	Week 12	n (%)	7 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	3 (42.86)	3 (60.00)
		Responders	4 (57.14)	2 (40.00)
		OR (95% CI)	2.00 (0.19, 20.61)	
		RR (95% CI)	1.43 (0.41, 4.99)	
		RD % (95% CI)	17.14 (-39.32, 73.60)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	7 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	3 (42.86)	3 (60.00)
		Responders	4 (57.14)	2 (40.00)
		OR (95% CI)	2.00 (0.19, 20.61)	
		RR (95% CI)	1.43 (0.41, 4.99)	
		RD % (95% CI)	17.14 (-39.32, 73.60)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) by region (patients with baseline GMFCS ≥ IV are excluded)

Region	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
Non-US	Week 12	n (%)	11 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (18.18)	0 (0.00)
		Non-Responders [2]	8 (72.73)	4 (100.00)
		Responders	3 (27.27)	0 (0.00)
		OR (95% CI)	3.71 (0.15, 88.75)	
		RR (95% CI)	2.92 (0.18, 46.71)	
		RD % (95% CI)	19.17 (-17.61, 55.95)	
		p-value – Fisher's Exact Test	0.5165	
	Week 24	n (%)	11 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (9.09)	0 (0.00)
		Non-Responders [2]	6 (54.55)	4 (100.00)
		Responders	5 (45.45)	0 (0.00)
		OR (95% CI)	7.62 (0.33, 175.01)	
		RR (95% CI)	4.58 (0.31, 68.24)	
		RD % (95% CI)	35.83 (-2.72, 74.38)	
		p-value – Fisher's Exact Test	0.2308	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.3.2.4 GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) by GMFCS (patients with baseline GMFCS ≥ IV are excluded)

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
All	Interaction test at Week 24	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.9720	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	6 (66.67)	5 (100.00)
		Responders	3 (33.33)	0 (0.00)
		OR (95% CI)	5.92 (0.25, 141.48)	
		RR (95% CI)	4.20 (0.26, 68.04)	
		RD % (95% CI)	26.67 (-10.25, 63.59)	
		p-value – Fisher's Exact Test	0.2582	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	6 (66.67)	5 (100.00)
		Responders	3 (33.33)	0 (0.00)
		OR (95% CI)	5.92 (0.25, 141.48)	
		RR (95% CI)	4.20 (0.26, 68.04)	
		RD % (95% CI)	26.67 (-10.25, 63.59)	
		p-value – Fisher's Exact Test	0.2582	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) by GMFCS (patients with baseline GMFCS ≥ IV are excluded)

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
≥ II	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	5 (55.56)	2 (50.00)
		Responders	4 (44.44)	2 (50.00)
		OR (95% CI)	0.80 (0.08, 8.47)	
		RR (95% CI)	0.89 (0.26, 3.02)	
		RD % (95% CI)	-5.56 (-64.33, 53.22)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	3 (33.33)	2 (50.00)
		Responders	6 (66.67)	2 (50.00)
		OR (95% CI)	2.00 (0.18, 22.06)	
		RR (95% CI)	1.33 (0.45, 3.94)	
		RD % (95% CI)	16.67 (-41.21, 74.54)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.3.2.5 GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) - excluding subject with data entry error by gender (patients with baseline GMFCS ≥ IV are excluded)

Gender	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
All	Interaction test at Week 24	Treatment*Gender, p-value Chi-Square[1]	0.9753	
Male	Week 12	n (%)	10 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (20.00)	0 (0.00)
		Non-Responders [2]	7 (70.00)	4 (66.67)
		Responders	3 (30.00)	2 (33.33)
		OR (95% CI)	0.86 (0.10, 7.51)	
		RR (95% CI)	0.90 (0.21, 3.94)	
		RD % (95% CI)	-3.33 (-50.55, 43.88)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	10 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (10.00)	0 (0.00)
		Non-Responders [2]	6 (60.00)	4 (66.67)
		Responders	4 (40.00)	2 (33.33)
		OR (95% CI)	1.33 (0.16, 11.07)	
		RR (95% CI)	1.20 (0.31, 4.69)	
		RD % (95% CI)	6.67 (-41.76, 55.09)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) - excluding subject with data entry error by gender (patients with baseline GMFCS ≥ IV are excluded)

Gender	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
Female	Week 12	n (%)	8 (100.00)	3 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	4 (50.00)	3 (100.00)
		Responders	4 (50.00)	0 (0.00)
		OR (95% CI)	7.00 (0.27, 178.47)	
		RR (95% CI)	4.00 (0.28, 57.98)	
		RD % (95% CI)	37.50 (-8.52, 83.52)	
		p-value – Fisher's Exact Test	0.2364	
	Week 24	n (%)	8 (100.00)	3 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	3 (37.50)	3 (100.00)
		Responders	5 (62.50)	0 (0.00)
		OR (95% CI)	11.00 (0.43, 284.30)	
		RR (95% CI)	4.89 (0.35, 68.83)	
		RD % (95% CI)	48.61 (3.17, 94.05)	
		p-value – Fisher's Exact Test	0.1818	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.3.2.6 GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) - excluding subject with data entry error by age group (patients with baseline GMFCS ≥ IV are excluded)

Age Group	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
All	Interaction test at Week 24	Treatment*Age Group, p-value Chi-Square[1]	0.9677	
<10.5 years old at screening	Week 12	n (%)	11 (100.00)	3 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (18.18)	0 (0.00)
		Non-Responders [2]	5 (45.45)	1 (33.33)
		Responders	6 (54.55)	2 (66.67)
		OR (95% CI)	0.60 (0.04, 8.73)	
		RR (95% CI)	0.82 (0.31, 2.15)	
		RD % (95% CI)	-12.12 (-73.04, 48.80)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	11 (100.00)	3 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (9.09)	0 (0.00)
		Non-Responders [2]	4 (36.36)	1 (33.33)
		Responders	7 (63.64)	2 (66.67)
		OR (95% CI)	0.88 (0.06, 12.97)	
		RR (95% CI)	0.95 (0.38, 2.39)	
		RD % (95% CI)	-3.03 (-63.48, 57.42)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) - excluding subject with data entry error by age group (patients with baseline GMFCS ≥ IV are excluded)

Age Group	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	7 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	6 (85.71)	6 (100.00)
		Responders	1 (14.29)	0 (0.00)
		OR (95% CI)	3.00 (0.10, 88.13)	
		RR (95% CI)	2.63 (0.13, 54.64)	
		RD % (95% CI)	11.61 (-21.49, 44.71)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	7 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	5 (71.43)	6 (100.00)
		Responders	2 (28.57)	0 (0.00)
		OR (95% CI)	5.91 (0.23, 151.15)	
		RR (95% CI)	4.38 (0.25, 76.54)	
		RD % (95% CI)	24.11 (-13.25, 61.47)	
		p-value – Fisher's Exact Test	0.4615	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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4.10.3.2.7 GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) - excluding subject with data entry error by region (patients with baseline GMFCS ≥ IV are excluded)

Region	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
All	Interaction test at Week 24	Treatment*Region, p-value Chi-Square[1]	0.9738	
US	Week 12	n (%)	7 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	3 (42.86)	3 (60.00)
		Responders	4 (57.14)	2 (40.00)
		OR (95% CI)	2.00 (0.19, 20.61)	
		RR (95% CI)	1.43 (0.41, 4.99)	
		RD % (95% CI)	17.14 (-39.32, 73.60)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	7 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	3 (42.86)	3 (60.00)
		Responders	4 (57.14)	2 (40.00)
		OR (95% CI)	2.00 (0.19, 20.61)	
		RR (95% CI)	1.43 (0.41, 4.99)	
		RD % (95% CI)	17.14 (-39.32, 73.60)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) - excluding subject with data entry error by region (patients with baseline GMFCS ≥ IV are excluded)

Region	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
Non-US	Week 12	n (%)	11 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (18.18)	0 (0.00)
		Non-Responders [2]	8 (72.73)	4 (100.00)
		Responders	3 (27.27)	0 (0.00)
		OR (95% CI)	3.71 (0.15, 88.75)	
		RR (95% CI)	2.92 (0.18, 46.71)	
		RD % (95% CI)	19.17 (-17.61, 55.95)	
		p-value – Fisher's Exact Test	0.5165	
	Week 24	n (%)	11 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (9.09)	0 (0.00)
		Non-Responders [2]	6 (54.55)	4 (100.00)
		Responders	5 (45.45)	0 (0.00)
		OR (95% CI)	7.62 (0.33, 175.01)	
		RR (95% CI)	4.58 (0.31, 68.24)	
		RD % (95% CI)	35.83 (-2.72, 74.38)	
		p-value – Fisher's Exact Test	0.2308	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.3.2.8 GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) - excluding subject with data entry error by GMFCS (patients with baseline GMFCS ≥ IV are excluded)

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
All	Interaction test at Week 24	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.9720	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	6 (66.67)	5 (100.00)
		Responders	3 (33.33)	0 (0.00)
		OR (95% CI)	5.92 (0.25, 141.48)	
		RR (95% CI)	4.20 (0.26, 68.04)	
		RD % (95% CI)	26.67 (-10.25, 63.59)	
		p-value – Fisher's Exact Test	0.2582	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	6 (66.67)	5 (100.00)
		Responders	3 (33.33)	0 (0.00)
		OR (95% CI)	5.92 (0.25, 141.48)	
		RR (95% CI)	4.20 (0.26, 68.04)	
		RD % (95% CI)	26.67 (-10.25, 63.59)	
		p-value – Fisher's Exact Test	0.2582	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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GMFM-E responders ≥ 4,0 (GMFCS I), 2,8 (GMFCS II) or 1,8 (GMFCS III) - excluding subject with data entry error by GMFCS (patients with baseline GMFCS ≥ IV are excluded)

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
≥ II	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	5 (55.56)	2 (50.00)
		Responders	4 (44.44)	2 (50.00)
		OR (95% CI)	0.80 (0.08, 8.47)	
		RR (95% CI)	0.89 (0.26, 3.02)	
		RD % (95% CI)	-5.56 (-64.33, 53.22)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	3 (33.33)	2 (50.00)
		Responders	6 (66.67)	2 (50.00)
		OR (95% CI)	2.00 (0.18, 22.06)	
		RR (95% CI)	1.33 (0.45, 3.94)	
		RD % (95% CI)	16.67 (-41.21, 74.54)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.4 Subgruppenanalysen für den Endpunkt GMFM-D

4.10.4.1 Analysen auf Basis des Full Analysis Set (inklusive Patienten mit Baseline-GMFCS ≥ IV)

4.10.4.1.1 GMFM-D by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.1894	
Male	Baseline	Absolute value	n (%)	12 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	27.92 (8.479)	26.43 (13.758)
	Week 12	Absolute value	n (%)	10 (83.33)	7 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	30.60 (7.575)	24.86 (15.421)
		Change from Baseline	n (%)	10 (83.33)	7 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	2.97 (1.008)	-1.58 (1.206)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	4.55 (1.573)	
			95% CI for LS Mean Difference [2]	1.17, 7.94	
			p-value MMRM [2]	0.0121 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.30	
			95% CI for SMD (Hedges' g)	0.23, 2.37	
			p-value WRS[3]	0.0062 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.
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1.4.4.1 GMFM-D
GMFM-D by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	11 (91.67)	7 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	30.64 (8.869)	27.00 (14.271)
		Change from Baseline	n (%)	11 (91.67)	7 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	3.28 (0.998)	0.56 (1.251)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.72 (1.601)	
			95% CI for LS Mean Difference [2]	-0.68, 6.12	
			p-value MMRM [2]	0.1095	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.76	
			95% CI for SMD (Hedges' g)	-0.23, 1.74	
			p-value WRS[3]	0.0961	
Female	Baseline	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	28.22 (11.487)	27.50 (18.628)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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1.4.4.1 GMFM-D
GMFM-D by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	8 (88.89)	3 (75.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (25.00)
			Mean (SD)	34.00 (4.106)	26.00 (15.716)
		Change from Baseline	n (%)	8 (88.89)	3 (75.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	1.96 (1.372)	0.93 (2.092)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.03 (2.499)	
			95% CI for LS Mean Difference [2]	-4.57, 6.64	
			p-value MMRM [2]	0.6886	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.23	
			95% CI for SMD (Hedges' g)	-1.10, 1.57	
			p-value WRS[3]	0.8667	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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1.4.4.1 GMFM-D
GMFM-D by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	30.22 (11.977)	30.25 (13.099)
		Change from Baseline	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	1.93 (1.331)	2.57 (1.999)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.64 (2.400)	
			95% CI for LS Mean Difference [2]	-5.99, 4.71	
			p-value MMRM [2]	0.7947	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.14	
			95% CI for SMD (Hedges' g)	-1.32, 1.04	
			p-value WRS[3]	1.0000	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.4.1.2 GMFM-D by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.2688	
<10.5 years old at screening	Baseline	Absolute value	n (%)	12 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	29.25 (6.982)	25.25 (17.076)
	Week 12	Absolute value	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	31.80 (5.095)	27.25 (12.971)
		Change from Baseline	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	2.96 (0.671)	1.18 (1.081)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.77 (1.282)	
			95% CI for LS Mean Difference [2]	-1.08, 4.63	
			p-value MMRM [2]	0.1968	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.73	
			95% CI for SMD (Hedges' g)	-0.46, 1.93	
			p-value WRS[3]	0.8092	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

NOTE: Median age used as cut-off point.

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GMFM-D by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	31.91 (5.974)	29.00 (12.437)
		Change from Baseline	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	3.31 (0.827)	2.93 (1.379)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.37 (1.613)	
			95% CI for LS Mean Difference [2]	-3.12, 3.87	
			p-value MMRM [2]	0.8200	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.12	
			95% CI for SMD (Hedges' g)	-1.02, 1.27	
			p-value WRS[3]	0.8256	
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	26.44 (12.601)	27.71 (14.660)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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GMFM-D by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	8 (88.89)	6 (85.71)
			Number of patients with missing data: n (%)	1 (11.11)	1 (14.29)
			Mean (SD)	32.50 (8.018)	23.83 (16.678)
		Change from Baseline	n (%)	8 (88.89)	6 (85.71)
			Number of patients with missing data: n (%)	1 (11.11)	1 (14.29)
			LS Mean Change from Baseline (SE) [2]	2.63 (1.302)	-2.09 (1.500)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	4.72 (1.986)	
			95% CI for LS Mean Difference [2]	0.43, 9.01	
			p-value MMRM [2]	0.0337 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.16	
			95% CI for SMD (Hedges' g)	0.01, 2.32	
			p-value WRS[3]	0.0320 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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GMFM-D by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	28.67 (13.811)	27.71 (14.694)
		Change from Baseline	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	2.24 (1.161)	-0.00 (1.314)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.25 (1.754)	
			95% CI for LS Mean Difference [2]	-1.54, 6.03	
			p-value MMRM [2]	0.2221	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.59	
			95% CI for SMD (Hedges' g)	-0.42, 1.60	
			p-value WRS[3]	0.4907	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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4.10.4.1.3 GMFM-D by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.4820	
US	Baseline	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	30.13 (7.954)	28.50 (14.279)
	Week 12	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	32.38 (6.632)	28.83 (14.372)
		Change from Baseline	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	2.28 (0.872)	0.29 (1.007)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.99 (1.334)	
			95% CI for LS Mean Difference [2]	-0.95, 4.93	
			p-value MMRM [2]	0.1640	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.72	
			95% CI for SMD (Hedges' g)	-0.38, 1.82	
			p-value WRS[3]	0.1758	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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GMFM-D by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	31.75 (8.664)	29.50 (14.802)
		Change from Baseline	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	1.66 (1.060)	0.96 (1.224)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.70 (1.621)	
			95% CI for LS Mean Difference [2]	-2.88, 4.28	
			p-value MMRM [2]	0.6746	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.21	
			95% CI for SMD (Hedges' g)	-0.85, 1.27	
			p-value WRS[3]	0.4972	
Non-US	Baseline	Absolute value	n (%)	13 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	26.77 (10.600)	24.80 (16.754)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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GMFM-D by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	10 (76.92)	4 (80.00)
			Number of patients with missing data: n (%)	3 (23.08)	1 (20.00)
			Mean (SD)	31.90 (6.471)	19.75 (15.196)
		Change from Baseline	n (%)	10 (76.92)	4 (80.00)
			Number of patients with missing data: n (%)	3 (23.08)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	3.02 (1.421)	-2.38 (2.231)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	5.40 (2.643)	
			95% CI for LS Mean Difference [2]	-0.35, 11.15	
			p-value MMRM [2]	0.0634	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.08	
			95% CI for SMD (Hedges' g)	-0.16, 2.32	
			p-value WRS[3]	0.1339	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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GMFM-D by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	12 (92.31)	5 (100.00)
			Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
			Mean (SD)	29.58 (11.229)	26.60 (12.700)
		Change from Baseline	n (%)	12 (92.31)	5 (100.00)
			Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	3.40 (1.189)	1.60 (1.847)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.80 (2.197)	
			95% CI for LS Mean Difference [2]	-2.91, 6.51	
			p-value MMRM [2]	0.4257	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.40	
			95% CI for SMD (Hedges' g)	-0.65, 1.45	
			p-value WRS[3]	0.2209	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.4.1.4 GMFM-D by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.7502	
I	Baseline	Absolute value	n (%)	9 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	32.89 (4.781)	37.00 (2.915)
	Week 12	Absolute value	n (%)	8 (88.89)	4 (80.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (20.00)
			Mean (SD)	34.88 (4.086)	36.00 (2.582)
		Change from Baseline	n (%)	8 (88.89)	4 (80.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	1.65 (0.883)	0.06 (1.216)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.59 (1.569)	
			95% CI for LS Mean Difference [2]	-1.87, 5.05	
			p-value MMRM [2]	0.3335	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.57	
			95% CI for SMD (Hedges' g)	-0.66, 1.79	
			p-value WRS[3]	0.2000	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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GMFM-D by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	35.13 (4.224)	37.60 (2.608)
		Change from Baseline	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	1.90 (0.814)	1.53 (1.084)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.37 (1.431)	
			95% CI for LS Mean Difference [2]	-2.81, 3.55	
			p-value MMRM [2]	0.8014	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.14	
			95% CI for SMD (Hedges' g)	-0.98, 1.26	
			p-value WRS[3]	0.4732	
≥ II	Baseline	Absolute value	n (%)	12 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	24.42 (10.850)	18.33 (15.462)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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GMFM-D by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	10 (83.33)	6 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	29.90 (7.141)	18.00 (15.007)
		Change from Baseline	n (%)	10 (83.33)	6 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	3.31 (1.345)	-0.75 (1.820)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	4.06 (2.303)	
			95% CI for LS Mean Difference [2]	-0.89, 9.01	
			p-value MMRM [2]	0.1002	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.85	
			95% CI for SMD (Hedges' g)	-0.21, 1.92	
			p-value WRS[3]	0.2083	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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GMFM-D by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	12 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	27.33 (11.750)	20.33 (13.589)
		Change from Baseline	n (%)	12 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	3.04 (1.307)	1.58 (1.887)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.46 (2.318)	
			95% CI for LS Mean Difference [2]	-3.47, 6.38	
			p-value MMRM [2]	0.5390	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.29	
			95% CI for SMD (Hedges' g)	-0.69, 1.28	
			p-value WRS[3]	0.5067	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.4.1.5 GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Gender, p-value Chi-Square[1]	0.9979	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	10 (83.33)	7 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	3.57 (0.15, 85.68)	
		RR (95% CI)	3.08 (0.17, 56.25)	
		RD % (95% CI)	12.98 (-14.23, 40.19)	
		p-value – Fisher's Exact Test	0.5088	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [2]	7 (58.33)	7 (100.00)
		Responders	5 (41.67)	0 (0.00)
		OR (95% CI)	11.00 (0.51, 236.22)	
		RR (95% CI)	6.77 (0.43, 106.72)	
		RD % (95% CI)	36.06 (4.39, 67.72)	
		p-value – Fisher's Exact Test	0.1060	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (25.00)
		Non-Responders [2]	7 (77.78)	4 (100.00)
		Responders	2 (22.22)	0 (0.00)
		OR (95% CI)	3.00 (0.12, 77.64)	
		RR (95% CI)	2.50 (0.15, 42.80)	
		RD % (95% CI)	15.00 (-22.57, 52.57)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	7 (77.78)	4 (100.00)
		Responders	2 (22.22)	0 (0.00)
		OR (95% CI)	3.00 (0.12, 77.64)	
		RR (95% CI)	2.50 (0.15, 42.80)	
		RD % (95% CI)	15.00 (-22.57, 52.57)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.4.1.6 GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Age Group, p-value Chi-Square[1]	1.0000	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	11 (91.67)	4 (100.00)
		Responders	1 (8.33)	0 (0.00)
		OR (95% CI)	1.17 (0.04, 34.52)	
		RR (95% CI)	1.15 (0.06, 23.88)	
		RD % (95% CI)	1.54 (-29.97, 33.05)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [2]	8 (66.67)	4 (100.00)
		Responders	4 (33.33)	0 (0.00)
		OR (95% CI)	4.76 (0.21, 109.78)	
		RR (95% CI)	3.46 (0.22, 53.27)	
		RD % (95% CI)	24.62 (-12.27, 61.50)	
		p-value – Fisher's Exact Test	0.5165	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (14.29)
		Non-Responders [2]	6 (66.67)	7 (100.00)
		Responders	3 (33.33)	0 (0.00)
		OR (95% CI)	8.08 (0.35, 187.32)	
		RR (95% CI)	5.60 (0.34, 93.35)	
		RD % (95% CI)	28.75 (-5.24, 62.74)	
		p-value – Fisher's Exact Test	0.2125	
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	6 (66.67)	7 (100.00)
		Responders	3 (33.33)	0 (0.00)
		OR (95% CI)	8.08 (0.35, 187.32)	
		RR (95% CI)	5.60 (0.34, 93.35)	
		RD % (95% CI)	28.75 (-5.24, 62.74)	
		p-value – Fisher's Exact Test	0.2125	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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4.10.4.1.7 GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Region, p-value Chi-Square[1]	0.9985	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	7 (87.50)	6 (100.00)
		Responders	1 (12.50)	0 (0.00)
		OR (95% CI)	2.60 (0.09, 75.49)	
		RR (95% CI)	2.33 (0.11, 48.99)	
		RD % (95% CI)	9.52 (-21.41, 40.46)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	6 (75.00)	6 (100.00)
		Responders	2 (25.00)	0 (0.00)
		OR (95% CI)	5.00 (0.20, 125.78)	
		RR (95% CI)	3.89 (0.22, 68.67)	
		RD % (95% CI)	20.63 (-14.30, 55.57)	
		p-value – Fisher's Exact Test	0.4725	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (23.08)	1 (20.00)
		Non-Responders [2]	10 (76.92)	5 (100.00)
		Responders	3 (23.08)	0 (0.00)
		OR (95% CI)	3.67 (0.16, 84.51)	
		RR (95% CI)	3.00 (0.18, 49.56)	
		RD % (95% CI)	16.67 (-15.01, 48.35)	
		p-value – Fisher's Exact Test	0.5221	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (7.69)	0 (0.00)
		Non-Responders [2]	8 (61.54)	5 (100.00)
		Responders	5 (38.46)	0 (0.00)
		OR (95% CI)	7.12 (0.32, 156.01)	
		RR (95% CI)	4.71 (0.31, 72.47)	
		RD % (95% CI)	30.95 (-2.86, 64.77)	
		p-value – Fisher's Exact Test	0.2489	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.4.1.8 GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	1.0000	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (20.00)
		Non-Responders [2]	7 (77.78)	5 (100.00)
		Responders	2 (22.22)	0 (0.00)
		OR (95% CI)	3.67 (0.15, 92.65)	
		RR (95% CI)	3.00 (0.17, 52.53)	
		RD % (95% CI)	16.67 (-18.11, 51.44)	
		p-value – Fisher's Exact Test	0.5055	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	6 (66.67)	5 (100.00)
		Responders	3 (33.33)	0 (0.00)
		OR (95% CI)	5.92 (0.25, 141.48)	
		RR (95% CI)	4.20 (0.26, 68.04)	
		RD % (95% CI)	26.67 (-10.25, 63.59)	
		p-value – Fisher's Exact Test	0.2582	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	10 (83.33)	6 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	3.10 (0.13, 75.18)	
		RR (95% CI)	2.69 (0.15, 48.64)	
		RD % (95% CI)	12.09 (-16.60, 40.78)	
		p-value – Fisher's Exact Test	0.5294	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	8 (66.67)	6 (100.00)
		Responders	4 (33.33)	0 (0.00)
		OR (95% CI)	6.88 (0.31, 152.02)	
		RR (95% CI)	4.85 (0.30, 77.61)	
		RD % (95% CI)	27.47 (-4.66, 59.61)	
		p-value – Fisher's Exact Test	0.2451	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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4.10.4.1.9 GMFM-D responders ≥ 5,9 by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Gender, p-value Chi-Square[1]	0.9754	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	11 (91.67)	7 (100.00)
		Responders	1 (8.33)	0 (0.00)
		OR (95% CI)	1.96 (0.07, 54.67)	
		RR (95% CI)	1.85 (0.09, 40.05)	
		RD % (95% CI)	5.29 (-18.86, 29.43)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [2]	10 (83.33)	7 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	3.57 (0.15, 85.68)	
		RR (95% CI)	3.08 (0.17, 56.25)	
		RD % (95% CI)	12.98 (-14.23, 40.19)	
		p-value – Fisher's Exact Test	0.5088	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
Table Generation: 11SEP2023 12:16:49 PM

GMFM-D responders ≥ 5,9 by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (25.00)
		Non-Responders [2]	7 (77.78)	3 (75.00)
		Responders	2 (22.22)	1 (25.00)
		OR (95% CI)	0.86 (0.05, 13.48)	
		RR (95% CI)	0.89 (0.11, 7.20)	
		RD % (95% CI)	-2.78 (-53.16, 47.60)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	7 (77.78)	3 (75.00)
		Responders	2 (22.22)	1 (25.00)
		OR (95% CI)	0.86 (0.05, 13.48)	
		RR (95% CI)	0.89 (0.11, 7.20)	
		RD % (95% CI)	-2.78 (-53.16, 47.60)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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4.10.4.1.10 GMFM-D responders ≥ 5,9 by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Age Group, p-value Chi-Square[1]	0.9740	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	10 (83.33)	3 (75.00)
		Responders	2 (16.67)	1 (25.00)
		OR (95% CI)	0.60 (0.04, 9.16)	
		RR (95% CI)	0.67 (0.08, 5.54)	
		RD % (95% CI)	-8.33 (-55.72, 39.05)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [2]	10 (83.33)	3 (75.00)
		Responders	2 (16.67)	1 (25.00)
		OR (95% CI)	0.60 (0.04, 9.16)	
		RR (95% CI)	0.67 (0.08, 5.54)	
		RD % (95% CI)	-8.33 (-55.72, 39.05)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
Program: t-qs-categ-sub.sas
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GMFM-D responders ≥ 5,9 by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (14.29)
		Non-Responders [2]	8 (88.89)	7 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	2.65 (0.09, 75.29)	
		RR (95% CI)	2.40 (0.11, 51.32)	
		RD % (95% CI)	8.75 (-19.02, 36.52)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	7 (77.78)	7 (100.00)
		Responders	2 (22.22)	0 (0.00)
		OR (95% CI)	5.00 (0.20, 122.74)	
		RR (95% CI)	4.00 (0.22, 72.01)	
		RD % (95% CI)	18.75 (-12.90, 50.40)	
		p-value – Fisher's Exact Test	0.4750	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
Program: t-qs-categ-sub.sas
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4.10.4.1.11 GMFM-D responders ≥ 5,9 by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Region, p-value Chi-Square[1]	0.9785	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	7 (87.50)	6 (100.00)
		Responders	1 (12.50)	0 (0.00)
		OR (95% CI)	2.60 (0.09, 75.49)	
		RR (95% CI)	2.33 (0.11, 48.99)	
		RD % (95% CI)	9.52 (-21.41, 40.46)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	7 (87.50)	6 (100.00)
		Responders	1 (12.50)	0 (0.00)
		OR (95% CI)	2.60 (0.09, 75.49)	
		RR (95% CI)	2.33 (0.11, 48.99)	
		RD % (95% CI)	9.52 (-21.41, 40.46)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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GMFM-D responders ≥ 5,9 by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (23.08)	1 (20.00)
		Non-Responders [2]	11 (84.62)	4 (80.00)
		Responders	2 (15.38)	1 (20.00)
		OR (95% CI)	0.73 (0.05, 10.39)	
		RR (95% CI)	0.77 (0.09, 6.72)	
		RD % (95% CI)	-4.62 (-44.79, 35.56)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (7.69)	0 (0.00)
		Non-Responders [2]	10 (76.92)	4 (80.00)
		Responders	3 (23.08)	1 (20.00)
		OR (95% CI)	1.20 (0.09, 15.26)	
		RR (95% CI)	1.15 (0.15, 8.65)	
		RD % (95% CI)	3.08 (-38.80, 44.96)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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4.10.4.1.12 GMFM-D responders ≥ 5,9 by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.9716	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (20.00)
		Non-Responders [2]	8 (88.89)	5 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	1.94 (0.07, 56.76)	
		RR (95% CI)	1.80 (0.09, 37.49)	
		RD % (95% CI)	6.67 (-24.62, 37.95)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	8 (88.89)	5 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	1.94 (0.07, 56.76)	
		RR (95% CI)	1.80 (0.09, 37.49)	
		RD % (95% CI)	6.67 (-24.62, 37.95)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
Table Generation: 11SEP2023 12:17:08 PM

GMFM-D responders ≥ 5,9 by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	10 (83.33)	5 (83.33)
		Responders	2 (16.67)	1 (16.67)
		OR (95% CI)	1.00 (0.07, 13.87)	
		RR (95% CI)	1.00 (0.11, 8.95)	
		RD % (95% CI)	0.00 (-36.52, 36.52)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	9 (75.00)	5 (83.33)
		Responders	3 (25.00)	1 (16.67)
		OR (95% CI)	1.67 (0.13, 20.58)	
		RR (95% CI)	1.50 (0.20, 11.54)	
		RD % (95% CI)	8.33 (-30.26, 46.93)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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4.10.4.1.13 GMFM-D - excluding subject with data entry error by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.6520	
Male	Baseline	Absolute value	n (%)	12 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	27.92 (8.479)	26.43 (13.758)
	Week 12	Absolute value	n (%)	10 (83.33)	7 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	30.60 (7.575)	24.86 (15.421)
		Change from Baseline	n (%)	10 (83.33)	7 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	2.97 (1.008)	-1.58 (1.206)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	4.55 (1.573)	
			95% CI for LS Mean Difference [2]	1.17, 7.94	
			p-value MMRM [2]	0.0121 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.30	
			95% CI for SMD (Hedges' g)	0.23, 2.37	
			p-value WRS[3]	0.0062 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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GMFM-D - excluding subject with data entry error by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	11 (91.67)	7 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	30.64 (8.869)	27.00 (14.271)
		Change from Baseline	n (%)	11 (91.67)	7 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	3.28 (0.998)	0.56 (1.251)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.72 (1.601)	
			95% CI for LS Mean Difference [2]	-0.68, 6.12	
			p-value MMRM [2]	0.1095	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.76	
			95% CI for SMD (Hedges' g)	-0.23, 1.74	
			p-value WRS[3]	0.0961	
Female	Baseline	Absolute value	n (%)	9 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			Mean (SD)	28.22 (11.487)	36.67 (4.041)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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GMFM-D - excluding subject with data entry error by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	8 (88.89)	2 (50.00)
			Number of patients with missing data: n (%)	1 (11.11)	2 (50.00)
			Mean (SD)	34.00 (4.106)	35.00 (2.828)
		Change from Baseline	n (%)	8 (88.89)	2 (50.00)
			Number of patients with missing data: n (%)	1 (11.11)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	1.94 (1.401)	-0.96 (2.479)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.90 (2.925)	
			95% CI for LS Mean Difference [2]	-3.67, 9.46	
			p-value MMRM [2]	0.3462	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.64	
			95% CI for SMD (Hedges' g)	-0.94, 2.22	
			p-value WRS[3]	0.5556	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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GMFM-D - excluding subject with data entry error by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	9 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			Mean (SD)	30.22 (11.977)	36.67 (3.215)
		Change from Baseline	n (%)	9 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	1.96 (1.253)	0.07 (2.174)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.90 (2.591)	
			95% CI for LS Mean Difference [2]	-3.96, 7.75	
			p-value MMRM [2]	0.4830	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.44	
			95% CI for SMD (Hedges' g)	-0.88, 1.76	
			p-value WRS[3]	0.5182	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.4.1.14 GMFM-D - excluding subject with data entry error by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.6544	
<10.5 years old at screening	Baseline	Absolute value	n (%)	12 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			Mean (SD)	29.25 (6.982)	33.67 (3.512)
	Week 12	Absolute value	n (%)	10 (83.33)	3 (75.00)
			Number of patients with missing data: n (%)	2 (16.67)	1 (25.00)
			Mean (SD)	31.80 (5.095)	33.67 (2.309)
		Change from Baseline	n (%)	10 (83.33)	3 (75.00)
			Number of patients with missing data: n (%)	2 (16.67)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	2.26 (0.662)	1.33 (1.268)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.93 (1.455)	
			95% CI for LS Mean Difference [2]	-2.33, 4.20	
			p-value MMRM [2]	0.5369	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.39	
			95% CI for SMD (Hedges' g)	-0.91, 1.69	
			p-value WRS[3]	0.3601	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

NOTE: Median age used as cut-off point.

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GMFM-D - excluding subject with data entry error by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	11 (91.67)	3 (75.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (25.00)
			Mean (SD)	31.91 (5.974)	35.00 (4.000)
		Change from Baseline	n (%)	11 (91.67)	3 (75.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	2.59 (0.902)	2.66 (1.745)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.08 (1.989)	
			95% CI for LS Mean Difference [2]	-4.45, 4.30	
			p-value MMRM [2]	0.9704	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.02	
			95% CI for SMD (Hedges' g)	-1.30, 1.25	
			p-value WRS[3]	0.2747	
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	26.44 (12.601)	27.71 (14.660)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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GMFM-D - excluding subject with data entry error by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	8 (88.89)	6 (85.71)
			Number of patients with missing data: n (%)	1 (11.11)	1 (14.29)
			Mean (SD)	32.50 (8.018)	23.83 (16.678)
		Change from Baseline	n (%)	8 (88.89)	6 (85.71)
			Number of patients with missing data: n (%)	1 (11.11)	1 (14.29)
			LS Mean Change from Baseline (SE) [2]	2.63 (1.302)	-2.09 (1.500)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	4.72 (1.986)	
			95% CI for LS Mean Difference [2]	0.43, 9.01	
			p-value MMRM [2]	0.0337 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.16	
			95% CI for SMD (Hedges' g)	0.01, 2.32	
			p-value WRS[3]	0.0320 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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GMFM-D - excluding subject with data entry error by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	28.67 (13.811)	27.71 (14.694)
		Change from Baseline	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	2.24 (1.161)	-0.00 (1.314)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.25 (1.754)	
			95% CI for LS Mean Difference [2]	-1.54, 6.03	
			p-value MMRM [2]	0.2221	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.59	
			95% CI for SMD (Hedges' g)	-0.42, 1.60	
			p-value WRS[3]	0.4907	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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4.10.4.1.15 GMFM-D - excluding subject with data entry error by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.1028	
US	Baseline	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	30.13 (7.954)	28.50 (14.279)
	Week 12	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	32.38 (6.632)	28.83 (14.372)
		Change from Baseline	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	2.28 (0.872)	0.29 (1.007)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.99 (1.334)	
			95% CI for LS Mean Difference [2]	-0.95, 4.93	
			p-value MMRM [2]	0.1640	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.72	
			95% CI for SMD (Hedges' g)	-0.38, 1.82	
			p-value WRS[3]	0.1758	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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GMFM-D - excluding subject with data entry error by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	31.75 (8.664)	29.50 (14.802)
		Change from Baseline	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	1.66 (1.060)	0.96 (1.224)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.70 (1.621)	
			95% CI for LS Mean Difference [2]	-2.88, 4.28	
			p-value MMRM [2]	0.6746	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.21	
			95% CI for SMD (Hedges' g)	-0.85, 1.27	
			p-value WRS[3]	0.4972	
Non-US	Baseline	Absolute value	n (%)	13 (100.00)	4 (80.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (20.00)
			Mean (SD)	26.77 (10.600)	31.00 (10.863)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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GMFM-D - excluding subject with data entry error by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	10 (76.92)	3 (60.00)
			Number of patients with missing data: n (%)	3 (23.08)	2 (40.00)
			Mean (SD)	31.90 (6.471)	23.67 (15.948)
		Change from Baseline	n (%)	10 (76.92)	3 (60.00)
			Number of patients with missing data: n (%)	3 (23.08)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	2.94 (1.218)	-4.75 (2.193)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	7.70 (2.513)	
			95% CI for LS Mean Difference [2]	2.16, 13.24	
			p-value MMRM [2]	0.0109 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.78	
			95% CI for SMD (Hedges' g)	0.29, 3.27	
			p-value WRS[3]	0.0035 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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GMFM-D - excluding subject with data entry error by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	12 (92.31)	4 (80.00)
			Number of patients with missing data: n (%)	1 (7.69)	1 (20.00)
			Mean (SD)	29.58 (11.229)	30.50 (10.661)
		Change from Baseline	n (%)	12 (92.31)	4 (80.00)
			Number of patients with missing data: n (%)	1 (7.69)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	3.39 (1.078)	-0.45 (1.861)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.84 (2.173)	
			95% CI for LS Mean Difference [2]	-0.86, 8.53	
			p-value MMRM [2]	0.1008	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.93	
			95% CI for SMD (Hedges' g)	-0.25, 2.12	
			p-value WRS[3]	0.0324 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
Program: t-qs-cont-sub.sas
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4.10.4.1.16 GMFM-D - excluding subject with data entry error by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.5110	
I	Baseline	Absolute value	n (%)	9 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	32.89 (4.781)	37.00 (2.915)
	Week 12	Absolute value	n (%)	8 (88.89)	4 (80.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (20.00)
			Mean (SD)	34.88 (4.086)	36.00 (2.582)
		Change from Baseline	n (%)	8 (88.89)	4 (80.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	1.65 (0.883)	0.06 (1.216)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.59 (1.569)	
			95% CI for LS Mean Difference [2]	-1.87, 5.05	
			p-value MMRM [2]	0.3335	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.57	
			95% CI for SMD (Hedges' g)	-0.66, 1.79	
			p-value WRS[3]	0.2000	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

Program: t-qs-cont-sub.sas

Table Generation: 11SEP2023 1:18:45 PM

GMFM-D - excluding subject with data entry error by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	35.13 (4.224)	37.60 (2.608)
		Change from Baseline	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	1.90 (0.814)	1.53 (1.084)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.37 (1.431)	
			95% CI for LS Mean Difference [2]	-2.81, 3.55	
			p-value MMRM [2]	0.8014	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.14	
			95% CI for SMD (Hedges' g)	-0.98, 1.26	
			p-value WRS[3]	0.4732	
≥ II	Baseline	Absolute value	n (%)	12 (100.00)	5 (83.33)
			Number of patients with missing data: n (%)	0 (0.00)	1 (16.67)
			Mean (SD)	24.42 (10.850)	22.00 (14.071)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
Program: t-qs-cont-sub.sas
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GMFM-D - excluding subject with data entry error by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	10 (83.33)	5 (83.33)
			Number of patients with missing data: n (%)	2 (16.67)	1 (16.67)
			Mean (SD)	29.90 (7.141)	20.00 (15.859)
		Change from Baseline	n (%)	10 (83.33)	5 (83.33)
			Number of patients with missing data: n (%)	2 (16.67)	1 (16.67)
			LS Mean Change from Baseline (SE) [2]	3.09 (1.227)	-2.03 (1.772)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	5.12 (2.166)	
			95% CI for LS Mean Difference [2]	0.40, 9.84	
			p-value MMRM [2]	0.0359 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.18	
			95% CI for SMD (Hedges' g)	0.02, 2.35	
			p-value WRS[3]	0.0496 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
Program: t-qs-cont-sub.sas
Table Generation: 11SEP2023 1:18:45 PM

GMFM-D - excluding subject with data entry error by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	12 (100.00)	5 (83.33)
			Number of patients with missing data: n (%)	0 (0.00)	1 (16.67)
			Mean (SD)	27.33 (11.750)	22.20 (14.307)
		Change from Baseline	n (%)	12 (100.00)	5 (83.33)
			Number of patients with missing data: n (%)	0 (0.00)	1 (16.67)
			LS Mean Change from Baseline (SE) [2]	2.92 (1.148)	0.17 (1.792)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.74 (2.128)	
			95% CI for LS Mean Difference [2]	-1.81, 7.30	
			p-value MMRM [2]	0.2179	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.63	
			95% CI for SMD (Hedges' g)	-0.44, 1.70	
			p-value WRS[3]	0.1660	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.4.1.17 GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) - excluding subject with data entry error by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Gender, p-value Chi-Square[1]	0.9979	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	10 (83.33)	7 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	3.57 (0.15, 85.68)	
		RR (95% CI)	3.08 (0.17, 56.25)	
		RD % (95% CI)	12.98 (-14.23, 40.19)	
		p-value – Fisher's Exact Test	0.5088	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [2]	7 (58.33)	7 (100.00)
		Responders	5 (41.67)	0 (0.00)
		OR (95% CI)	11.00 (0.51, 236.22)	
		RR (95% CI)	6.77 (0.43, 106.72)	
		RD % (95% CI)	36.06 (4.39, 67.72)	
		p-value – Fisher's Exact Test	0.1060	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) - excluding subject with data entry error by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	2 (50.00)
		Non-Responders [2]	7 (77.78)	4 (100.00)
		Responders	2 (22.22)	0 (0.00)
		OR (95% CI)	3.00 (0.12, 77.64)	
		RR (95% CI)	2.50 (0.15, 42.80)	
		RD % (95% CI)	15.00 (-22.57, 52.57)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	1 (25.00)
		Non-Responders [2]	7 (77.78)	4 (100.00)
		Responders	2 (22.22)	0 (0.00)
		OR (95% CI)	3.00 (0.12, 77.64)	
		RR (95% CI)	2.50 (0.15, 42.80)	
		RD % (95% CI)	15.00 (-22.57, 52.57)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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4.10.4.1.18 GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) - excluding subject with data entry error by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Age Group, p-value Chi-Square[1]	1.0000	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (25.00)
		Non-Responders [2]	11 (91.67)	4 (100.00)
		Responders	1 (8.33)	0 (0.00)
		OR (95% CI)	1.17 (0.04, 34.52)	
		RR (95% CI)	1.15 (0.06, 23.88)	
		RD % (95% CI)	1.54 (-29.97, 33.05)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	1 (25.00)
		Non-Responders [2]	8 (66.67)	4 (100.00)
		Responders	4 (33.33)	0 (0.00)
		OR (95% CI)	4.76 (0.21, 109.78)	
		RR (95% CI)	3.46 (0.22, 53.27)	
		RD % (95% CI)	24.62 (-12.27, 61.50)	
		p-value – Fisher's Exact Test	0.5165	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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Table Generation: 11SEP2023 12:17:20 PM

GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) - excluding subject with data entry error by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (14.29)
		Non-Responders [2]	6 (66.67)	7 (100.00)
		Responders	3 (33.33)	0 (0.00)
		OR (95% CI)	8.08 (0.35, 187.32)	
		RR (95% CI)	5.60 (0.34, 93.35)	
		RD % (95% CI)	28.75 (-5.24, 62.74)	
		p-value – Fisher's Exact Test	0.2125	
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	6 (66.67)	7 (100.00)
		Responders	3 (33.33)	0 (0.00)
		OR (95% CI)	8.08 (0.35, 187.32)	
		RR (95% CI)	5.60 (0.34, 93.35)	
		RD % (95% CI)	28.75 (-5.24, 62.74)	
		p-value – Fisher's Exact Test	0.2125	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
Program: t-qs-categ-sub.sas
Table Generation: 11SEP2023 12:17:20 PM

4.10.4.1.19 GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) - excluding subject with data entry error by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Region, p-value Chi-Square[1]	0.9985	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	7 (87.50)	6 (100.00)
		Responders	1 (12.50)	0 (0.00)
		OR (95% CI)	2.60 (0.09, 75.49)	
		RR (95% CI)	2.33 (0.11, 48.99)	
		RD % (95% CI)	9.52 (-21.41, 40.46)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	6 (75.00)	6 (100.00)
		Responders	2 (25.00)	0 (0.00)
		OR (95% CI)	5.00 (0.20, 125.78)	
		RR (95% CI)	3.89 (0.22, 68.67)	
		RD % (95% CI)	20.63 (-14.30, 55.57)	
		p-value – Fisher's Exact Test	0.4725	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) - excluding subject with data entry error by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (23.08)	2 (40.00)
		Non-Responders [2]	10 (76.92)	5 (100.00)
		Responders	3 (23.08)	0 (0.00)
		OR (95% CI)	3.67 (0.16, 84.51)	
		RR (95% CI)	3.00 (0.18, 49.56)	
		RD % (95% CI)	16.67 (-15.01, 48.35)	
		p-value – Fisher's Exact Test	0.5221	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (7.69)	1 (20.00)
		Non-Responders [2]	8 (61.54)	5 (100.00)
		Responders	5 (38.46)	0 (0.00)
		OR (95% CI)	7.12 (0.32, 156.01)	
		RR (95% CI)	4.71 (0.31, 72.47)	
		RD % (95% CI)	30.95 (-2.86, 64.77)	
		p-value – Fisher's Exact Test	0.2489	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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4.10.4.1.20 GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) - excluding subject with data entry error by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	1.0000	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (20.00)
		Non-Responders [2]	7 (77.78)	5 (100.00)
		Responders	2 (22.22)	0 (0.00)
		OR (95% CI)	3.67 (0.15, 92.65)	
		RR (95% CI)	3.00 (0.17, 52.53)	
		RD % (95% CI)	16.67 (-18.11, 51.44)	
		p-value – Fisher's Exact Test	0.5055	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	6 (66.67)	5 (100.00)
		Responders	3 (33.33)	0 (0.00)
		OR (95% CI)	5.92 (0.25, 141.48)	
		RR (95% CI)	4.20 (0.26, 68.04)	
		RD % (95% CI)	26.67 (-10.25, 63.59)	
		p-value – Fisher's Exact Test	0.2582	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) - excluding subject with data entry error by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (16.67)
		Non-Responders [2]	10 (83.33)	6 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	3.10 (0.13, 75.18)	
		RR (95% CI)	2.69 (0.15, 48.64)	
		RD % (95% CI)	12.09 (-16.60, 40.78)	
		p-value – Fisher's Exact Test	0.5294	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	1 (16.67)
		Non-Responders [2]	8 (66.67)	6 (100.00)
		Responders	4 (33.33)	0 (0.00)
		OR (95% CI)	6.88 (0.31, 152.02)	
		RR (95% CI)	4.85 (0.30, 77.61)	
		RD % (95% CI)	27.47 (-4.66, 59.61)	
		p-value – Fisher's Exact Test	0.2451	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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4.10.4.1.21 GMFM-D responders ≥ 5,9 - excluding subject with data entry error by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Gender, p-value Chi-Square[1]	0.9994	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	11 (91.67)	7 (100.00)
		Responders	1 (8.33)	0 (0.00)
		OR (95% CI)	1.96 (0.07, 54.67)	
		RR (95% CI)	1.85 (0.09, 40.05)	
		RD % (95% CI)	5.29 (-18.86, 29.43)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [2]	10 (83.33)	7 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	3.57 (0.15, 85.68)	
		RR (95% CI)	3.08 (0.17, 56.25)	
		RD % (95% CI)	12.98 (-14.23, 40.19)	
		p-value – Fisher's Exact Test	0.5088	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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GMFM-D responders ≥ 5,9 - excluding subject with data entry error by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	2 (50.00)
		Non-Responders [2]	7 (77.78)	4 (100.00)
		Responders	2 (22.22)	0 (0.00)
		OR (95% CI)	3.00 (0.12, 77.64)	
		RR (95% CI)	2.50 (0.15, 42.80)	
		RD % (95% CI)	15.00 (-22.57, 52.57)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	1 (25.00)
		Non-Responders [2]	7 (77.78)	4 (100.00)
		Responders	2 (22.22)	0 (0.00)
		OR (95% CI)	3.00 (0.12, 77.64)	
		RR (95% CI)	2.50 (0.15, 42.80)	
		RD % (95% CI)	15.00 (-22.57, 52.57)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
Table Generation: 11SEP2023 12:18:04 PM

4.10.4.1.22 GMFM-D responders ≥ 5,9 - excluding subject with data entry error by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Age Group, p-value Chi-Square[1]	0.9994	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (25.00)
		Non-Responders [2]	10 (83.33)	4 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	2.14 (0.08, 54.22)	
		RR (95% CI)	1.92 (0.11, 33.44)	
		RD % (95% CI)	9.23 (-24.69, 43.15)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	1 (25.00)
		Non-Responders [2]	10 (83.33)	4 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	2.14 (0.08, 54.22)	
		RR (95% CI)	1.92 (0.11, 33.44)	
		RD % (95% CI)	9.23 (-24.69, 43.15)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
Program: t-qs-categ-sub.sas
Table Generation: 11SEP2023 12:18:10 PM

GMFM-D responders ≥ 5,9 - excluding subject with data entry error by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (14.29)
		Non-Responders [2]	8 (88.89)	7 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	2.65 (0.09, 75.29)	
		RR (95% CI)	2.40 (0.11, 51.32)	
		RD % (95% CI)	8.75 (-19.02, 36.52)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	7 (77.78)	7 (100.00)
		Responders	2 (22.22)	0 (0.00)
		OR (95% CI)	5.00 (0.20, 122.74)	
		RR (95% CI)	4.00 (0.22, 72.01)	
		RD % (95% CI)	18.75 (-12.90, 50.40)	
		p-value – Fisher's Exact Test	0.4750	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
Program: t-qs-categ-sub.sas
Table Generation: 11SEP2023 12:18:10 PM

4.10.4.1.23 GMFM-D responders ≥ 5,9 - excluding subject with data entry error by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Region, p-value Chi-Square[1]	0.9986	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	7 (87.50)	6 (100.00)
		Responders	1 (12.50)	0 (0.00)
		OR (95% CI)	2.60 (0.09, 75.49)	
		RR (95% CI)	2.33 (0.11, 48.99)	
		RD % (95% CI)	9.52 (-21.41, 40.46)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	7 (87.50)	6 (100.00)
		Responders	1 (12.50)	0 (0.00)
		OR (95% CI)	2.60 (0.09, 75.49)	
		RR (95% CI)	2.33 (0.11, 48.99)	
		RD % (95% CI)	9.52 (-21.41, 40.46)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
Table Generation: 11SEP2023 12:18:19 PM

GMFM-D responders ≥ 5,9 - excluding subject with data entry error by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (23.08)	2 (40.00)
		Non-Responders [2]	11 (84.62)	5 (100.00)
		Responders	2 (15.38)	0 (0.00)
		OR (95% CI)	2.39 (0.10, 58.77)	
		RR (95% CI)	2.14 (0.12, 38.24)	
		RD % (95% CI)	9.52 (-20.34, 39.38)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (7.69)	1 (20.00)
		Non-Responders [2]	10 (76.92)	5 (100.00)
		Responders	3 (23.08)	0 (0.00)
		OR (95% CI)	3.67 (0.16, 84.51)	
		RR (95% CI)	3.00 (0.18, 49.56)	
		RD % (95% CI)	16.67 (-15.01, 48.35)	
		p-value – Fisher's Exact Test	0.5221	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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4.10.4.1.24 GMFM-D responders ≥ 5,9 - excluding subject with data entry error by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.9982	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (20.00)
		Non-Responders [2]	8 (88.89)	5 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	1.94 (0.07, 56.76)	
		RR (95% CI)	1.80 (0.09, 37.49)	
		RD % (95% CI)	6.67 (-24.62, 37.95)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	8 (88.89)	5 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	1.94 (0.07, 56.76)	
		RR (95% CI)	1.80 (0.09, 37.49)	
		RD % (95% CI)	6.67 (-24.62, 37.95)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
Table Generation: 11SEP2023 12:18:52 PM

GMFM-D responders ≥ 5,9 - excluding subject with data entry error by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (16.67)
		Non-Responders [2]	10 (83.33)	6 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	3.10 (0.13, 75.18)	
		RR (95% CI)	2.69 (0.15, 48.64)	
		RD % (95% CI)	12.09 (-16.60, 40.78)	
		p-value – Fisher's Exact Test	0.5294	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	1 (16.67)
		Non-Responders [2]	9 (75.00)	6 (100.00)
		Responders	3 (25.00)	0 (0.00)
		OR (95% CI)	4.79 (0.21, 109.19)	
		RR (95% CI)	3.77 (0.23, 63.05)	
		RD % (95% CI)	19.78 (-10.97, 50.53)	
		p-value – Fisher's Exact Test	0.5147	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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4.10.4.2 Analysen unter Ausschluss von Patienten mit Baseline-GMFCS ≥ IV

4.10.4.2.1 GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) by gender (patients with baseline GMFCS ≥ IV are excluded)

Gender	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
All	Interaction test at Week 24	Treatment*Gender, p-value Chi-Square[1]	0.9977	
Male	Week 12	n (%)	10 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (20.00)	0 (0.00)
		Non-Responders [2]	8 (80.00)	6 (100.00)
		Responders	2 (20.00)	0 (0.00)
		OR (95% CI)	3.82 (0.16, 94.13)	
		RR (95% CI)	3.18 (0.18, 56.95)	
		RD % (95% CI)	15.58 (-15.68, 46.85)	
		p-value – Fisher's Exact Test	0.5000	
	Week 24	n (%)	10 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (10.00)	0 (0.00)
		Non-Responders [2]	5 (50.00)	6 (100.00)
		Responders	5 (50.00)	0 (0.00)
		OR (95% CI)	13.00 (0.58, 291.41)	
		RR (95% CI)	7.00 (0.45, 107.93)	
		RD % (95% CI)	42.86 (7.69, 78.03)	
		p-value – Fisher's Exact Test	0.0934	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.

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1.4.13 Sensitivity analyses for GMFM-D
GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) by gender (patients with baseline GMFCS ≥ IV are excluded)

Gender	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
Female	Week 12	n (%)	8 (100.00)	3 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	1 (33.33)
		Non-Responders [2]	6 (75.00)	3 (100.00)
		Responders	2 (25.00)	0 (0.00)
		OR (95% CI)	2.69 (0.10, 73.20)	
		RR (95% CI)	2.22 (0.14, 36.49)	
		RD % (95% CI)	15.28 (-28.39, 58.94)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	8 (100.00)	3 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	6 (75.00)	3 (100.00)
		Responders	2 (25.00)	0 (0.00)
		OR (95% CI)	2.69 (0.10, 73.20)	
		RR (95% CI)	2.22 (0.14, 36.49)	
		RD % (95% CI)	15.28 (-28.39, 58.94)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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4.10.4.2.2 GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) by age group (patients with baseline GMFCS ≥ IV are excluded)

Age Group	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
All	Interaction test at Week 24	Treatment*Age Group, p-value Chi-Square[1]	0.9994	
<10.5 years old at screening	Week 12	n (%)	11 (100.00)	3 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (18.18)	0 (0.00)
		Non-Responders [2]	10 (90.91)	3 (100.00)
		Responders	1 (9.09)	0 (0.00)
		OR (95% CI)	1.00 (0.03, 30.62)	
		RR (95% CI)	1.00 (0.05, 19.96)	
		RD % (95% CI)	0.00 (-37.42, 37.42)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	11 (100.00)	3 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (9.09)	0 (0.00)
		Non-Responders [2]	7 (63.64)	3 (100.00)
		Responders	4 (36.36)	0 (0.00)
		OR (95% CI)	4.20 (0.17, 101.54)	
		RR (95% CI)	3.00 (0.20, 44.36)	
		RD % (95% CI)	25.00 (-17.43, 67.43)	
		p-value – Fisher's Exact Test	0.5055	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) by age group (patients with baseline GMFCS ≥ IV are excluded)

Age Group	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	7 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	1 (16.67)
		Non-Responders [2]	4 (57.14)	6 (100.00)
		Responders	3 (42.86)	0 (0.00)
		OR (95% CI)	10.11 (0.41, 247.48)	
		RR (95% CI)	6.13 (0.38, 99.14)	
		RD % (95% CI)	36.61 (-2.71, 75.92)	
		p-value – Fisher's Exact Test	0.1923	
	Week 24	n (%)	7 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	4 (57.14)	6 (100.00)
		Responders	3 (42.86)	0 (0.00)
		OR (95% CI)	10.11 (0.41, 247.48)	
		RR (95% CI)	6.13 (0.38, 99.14)	
		RD % (95% CI)	36.61 (-2.71, 75.92)	
		p-value – Fisher's Exact Test	0.1923	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
Program: t-qs-categ-sub.sas
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4.10.4.2.3 GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) by region (patients with baseline GMFCS ≥ IV are excluded)

Region	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
All	Interaction test at Week 24	Treatment*Region, p-value Chi-Square[1]	0.9983	
US	Week 12	n (%)	7 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	6 (85.71)	5 (100.00)
		Responders	1 (14.29)	0 (0.00)
		OR (95% CI)	2.54 (0.09, 75.76)	
		RR (95% CI)	2.25 (0.11, 46.13)	
		RD % (95% CI)	10.42 (-24.52, 45.35)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	7 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	5 (71.43)	5 (100.00)
		Responders	2 (28.57)	0 (0.00)
		OR (95% CI)	5.00 (0.19, 130.02)	
		RR (95% CI)	3.75 (0.22, 64.56)	
		RD % (95% CI)	22.92 (-16.08, 61.91)	
		p-value – Fisher's Exact Test	0.4697	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) by region (patients with baseline GMFCS ≥ IV are excluded)

Region	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
Non-US	Week 12	n (%)	11 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (18.18)	1 (25.00)
		Non-Responders [2]	8 (72.73)	4 (100.00)
		Responders	3 (27.27)	0 (0.00)
		OR (95% CI)	3.71 (0.15, 88.75)	
		RR (95% CI)	2.92 (0.18, 46.71)	
		RD % (95% CI)	19.17 (-17.61, 55.95)	
		p-value – Fisher's Exact Test	0.5165	
	Week 24	n (%)	11 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (9.09)	0 (0.00)
		Non-Responders [2]	6 (54.55)	4 (100.00)
		Responders	5 (45.45)	0 (0.00)
		OR (95% CI)	7.62 (0.33, 175.01)	
		RR (95% CI)	4.58 (0.31, 68.24)	
		RD % (95% CI)	35.83 (-2.72, 74.38)	
		p-value – Fisher's Exact Test	0.2308	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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4.10.4.2.4 GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) by GMFCS (patients with baseline GMFCS ≥ IV are excluded)

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
All	Interaction test at Week 24	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.9989	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (20.00)
		Non-Responders [2]	7 (77.78)	5 (100.00)
		Responders	2 (22.22)	0 (0.00)
		OR (95% CI)	3.67 (0.15, 92.65)	
		RR (95% CI)	3.00 (0.17, 52.53)	
		RD % (95% CI)	16.67 (-18.11, 51.44)	
		p-value – Fisher's Exact Test	0.5055	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	6 (66.67)	5 (100.00)
		Responders	3 (33.33)	0 (0.00)
		OR (95% CI)	5.92 (0.25, 141.48)	
		RR (95% CI)	4.20 (0.26, 68.04)	
		RD % (95% CI)	26.67 (-10.25, 63.59)	
		p-value – Fisher's Exact Test	0.2582	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) by GMFCS (patients with baseline GMFCS ≥ IV are excluded)

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
≥ II	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	7 (77.78)	4 (100.00)
		Responders	2 (22.22)	0 (0.00)
		OR (95% CI)	3.00 (0.12, 77.64)	
		RR (95% CI)	2.50 (0.15, 42.80)	
		RD % (95% CI)	15.00 (-22.57, 52.57)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	5 (55.56)	4 (100.00)
		Responders	4 (44.44)	0 (0.00)
		OR (95% CI)	7.36 (0.31, 176.41)	
		RR (95% CI)	4.50 (0.30, 68.13)	
		RD % (95% CI)	35.00 (-5.52, 75.52)	
		p-value – Fisher's Exact Test	0.2280	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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4.10.4.2.5 GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) - excluding subject with data entry error by gender (patients with baseline GMFCS ≥ IV are excluded)

Gender	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
All	Interaction test at Week 24	Treatment*Gender, p-value Chi-Square[1]	0.9977	
Male	Week 12	n (%)	10 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (20.00)	0 (0.00)
		Non-Responders [2]	8 (80.00)	6 (100.00)
		Responders	2 (20.00)	0 (0.00)
		OR (95% CI)	3.82 (0.16, 94.13)	
		RR (95% CI)	3.18 (0.18, 56.95)	
		RD % (95% CI)	15.58 (-15.68, 46.85)	
		p-value – Fisher's Exact Test	0.5000	
	Week 24	n (%)	10 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (10.00)	0 (0.00)
		Non-Responders [2]	5 (50.00)	6 (100.00)
		Responders	5 (50.00)	0 (0.00)
		OR (95% CI)	13.00 (0.58, 291.41)	
		RR (95% CI)	7.00 (0.45, 107.93)	
		RD % (95% CI)	42.86 (7.69, 78.03)	
		p-value – Fisher's Exact Test	0.0934	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) - excluding subject with data entry error by gender (patients with baseline GMFCS ≥ IV are excluded)

Gender	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
Female	Week 12	n (%)	8 (100.00)	3 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	1 (33.33)
		Non-Responders [2]	6 (75.00)	3 (100.00)
		Responders	2 (25.00)	0 (0.00)
		OR (95% CI)	2.69 (0.10, 73.20)	
		RR (95% CI)	2.22 (0.14, 36.49)	
		RD % (95% CI)	15.28 (-28.39, 58.94)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	8 (100.00)	3 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	6 (75.00)	3 (100.00)
		Responders	2 (25.00)	0 (0.00)
		OR (95% CI)	2.69 (0.10, 73.20)	
		RR (95% CI)	2.22 (0.14, 36.49)	
		RD % (95% CI)	15.28 (-28.39, 58.94)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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4.10.4.2.6 GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) - excluding subject with data entry error by age group (patients with baseline GMFCS ≥ IV are excluded)

Age Group	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
All	Interaction test at Week 24	Treatment*Age Group, p-value Chi-Square[1]	0.9994	
<10.5 years old at screening	Week 12	n (%)	11 (100.00)	3 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (18.18)	0 (0.00)
		Non-Responders [2]	10 (90.91)	3 (100.00)
		Responders	1 (9.09)	0 (0.00)
		OR (95% CI)	1.00 (0.03, 30.62)	
		RR (95% CI)	1.00 (0.05, 19.96)	
		RD % (95% CI)	0.00 (-37.42, 37.42)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	11 (100.00)	3 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (9.09)	0 (0.00)
		Non-Responders [2]	7 (63.64)	3 (100.00)
		Responders	4 (36.36)	0 (0.00)
		OR (95% CI)	4.20 (0.17, 101.54)	
		RR (95% CI)	3.00 (0.20, 44.36)	
		RD % (95% CI)	25.00 (-17.43, 67.43)	
		p-value – Fisher's Exact Test	0.5055	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) - excluding subject with data entry error by age group (patients with baseline GMFCS ≥ IV are excluded)

Age Group	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	7 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	1 (16.67)
		Non-Responders [2]	4 (57.14)	6 (100.00)
		Responders	3 (42.86)	0 (0.00)
		OR (95% CI)	10.11 (0.41, 247.48)	
		RR (95% CI)	6.13 (0.38, 99.14)	
		RD % (95% CI)	36.61 (-2.71, 75.92)	
		p-value – Fisher's Exact Test	0.1923	
	Week 24	n (%)	7 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	4 (57.14)	6 (100.00)
		Responders	3 (42.86)	0 (0.00)
		OR (95% CI)	10.11 (0.41, 247.48)	
		RR (95% CI)	6.13 (0.38, 99.14)	
		RD % (95% CI)	36.61 (-2.71, 75.92)	
		p-value – Fisher's Exact Test	0.1923	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
Program: t-qs-categ-sub.sas
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4.10.4.2.7 GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) - excluding subject with data entry error by region (patients with baseline GMFCS ≥ IV are excluded)

Region	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
All	Interaction test at Week 24	Treatment*Region, p-value Chi-Square[1]	0.9983	
US	Week 12	n (%)	7 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	6 (85.71)	5 (100.00)
		Responders	1 (14.29)	0 (0.00)
		OR (95% CI)	2.54 (0.09, 75.76)	
		RR (95% CI)	2.25 (0.11, 46.13)	
		RD % (95% CI)	10.42 (-24.52, 45.35)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	7 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	5 (71.43)	5 (100.00)
		Responders	2 (28.57)	0 (0.00)
		OR (95% CI)	5.00 (0.19, 130.02)	
		RR (95% CI)	3.75 (0.22, 64.56)	
		RD % (95% CI)	22.92 (-16.08, 61.91)	
		p-value – Fisher's Exact Test	0.4697	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) - excluding subject with data entry error by region (patients with baseline GMFCS ≥ IV are excluded)

Region	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
Non-US	Week 12	n (%)	11 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (18.18)	1 (25.00)
		Non-Responders [2]	8 (72.73)	4 (100.00)
		Responders	3 (27.27)	0 (0.00)
		OR (95% CI)	3.71 (0.15, 88.75)	
		RR (95% CI)	2.92 (0.18, 46.71)	
		RD % (95% CI)	19.17 (-17.61, 55.95)	
		p-value – Fisher's Exact Test	0.5165	
	Week 24	n (%)	11 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (9.09)	0 (0.00)
		Non-Responders [2]	6 (54.55)	4 (100.00)
		Responders	5 (45.45)	0 (0.00)
		OR (95% CI)	7.62 (0.33, 175.01)	
		RR (95% CI)	4.58 (0.31, 68.24)	
		RD % (95% CI)	35.83 (-2.72, 74.38)	
		p-value – Fisher's Exact Test	0.2308	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
Table Generation: 11SEP2023 12:26:08 PM

4.10.4.2.8 GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) - excluding subject with data entry error by GMFCS (patients with baseline GMFCS ≥ IV are excluded)

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
All	Interaction test at Week 24	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.9989	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (20.00)
		Non-Responders [2]	7 (77.78)	5 (100.00)
		Responders	2 (22.22)	0 (0.00)
		OR (95% CI)	3.67 (0.15, 92.65)	
		RR (95% CI)	3.00 (0.17, 52.53)	
		RD % (95% CI)	16.67 (-18.11, 51.44)	
		p-value – Fisher's Exact Test	0.5055	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	6 (66.67)	5 (100.00)
		Responders	3 (33.33)	0 (0.00)
		OR (95% CI)	5.92 (0.25, 141.48)	
		RR (95% CI)	4.20 (0.26, 68.04)	
		RD % (95% CI)	26.67 (-10.25, 63.59)	
		p-value – Fisher's Exact Test	0.2582	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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GMFM-D responders ≥ 2,4 (GMFCS I), 3,3 (GMFCS II) or 1,5 (GMFCS III) - excluding subject with data entry error by GMFCS (patients with baseline GMFCS ≥ IV are excluded)

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
≥ II	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	7 (77.78)	4 (100.00)
		Responders	2 (22.22)	0 (0.00)
		OR (95% CI)	3.00 (0.12, 77.64)	
		RR (95% CI)	2.50 (0.15, 42.80)	
		RD % (95% CI)	15.00 (-22.57, 52.57)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	5 (55.56)	4 (100.00)
		Responders	4 (44.44)	0 (0.00)
		OR (95% CI)	7.36 (0.31, 176.41)	
		RR (95% CI)	4.50 (0.30, 68.13)	
		RD % (95% CI)	35.00 (-5.52, 75.52)	
		p-value – Fisher's Exact Test	0.2280	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.5 Subgruppenanalysen für den kombinierten Mobilitätsendpunkt

4.10.5.1 Composite clinical outcomes responders - improvement in at least 1 of the 3 component assessments by gender

Gender	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
All	Interaction	Treatment*Gender, p-value Chi-Square[1]	0.6511	
Male	Week 12	n (%)	10 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (20.00)	0 (0.00)
		Non-Responders [1]	5 (50.00)	4 (66.67)
		Responders	5 (50.00)	2 (33.33)
		OR (95% CI)	2.00 (0.24, 16.36)	
		RR (95% CI)	1.50 (0.41, 5.45)	
		RD % (95% CI)	16.67 (-32.15, 65.48)	
		p-value – Fisher's Exact Test	0.6329	
	Week 24	n (%)	10 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (10.00)	0 (0.00)
		Non-Responders [1]	4 (40.00)	3 (50.00)
		Responders	6 (60.00)	3 (50.00)
		OR (95% CI)	1.50 (0.20, 11.54)	
		RR (95% CI)	1.20 (0.47, 3.09)	
		RD % (95% CI)	10.00 (-40.23, 60.23)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.

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1.4.5 Composite clinical outcomes
Composite clinical outcomes responders - improvement in at least 1 of the 3 component assessments by gender

Gender	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
Female	Week 12	n (%)	8 (100.00)	3 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	3 (37.50)	2 (66.67)
		Responders	5 (62.50)	1 (33.33)
		OR (95% CI)	3.33 (0.20, 54.53)	
		RR (95% CI)	1.88 (0.35, 10.14)	
		RD % (95% CI)	29.17 (-33.85, 92.18)	
		p-value – Fisher's Exact Test	0.5455	
	Week 24	n (%)	8 (100.00)	3 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	3 (37.50)	2 (66.67)
		Responders	5 (62.50)	1 (33.33)
		OR (95% CI)	3.33 (0.20, 54.53)	
		RR (95% CI)	1.88 (0.35, 10.14)	
		RD % (95% CI)	29.17 (-33.85, 92.18)	
		p-value – Fisher's Exact Test	0.5455	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.5.2 Composite clinical outcomes responders - improvement in at least 1 of the 3 component assessments by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
All	Interaction	Treatment*Age Group, p-value Chi-Square[1]	0.9482	
<10.5 years old at screening	Week 12	n (%)	11 (100.00)	3 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (18.18)	0 (0.00)
		Non-Responders [1]	5 (45.45)	1 (33.33)
		Responders	6 (54.55)	2 (66.67)
		OR (95% CI)	0.60 (0.04, 8.73)	
		RR (95% CI)	0.82 (0.31, 2.15)	
		RD % (95% CI)	-12.12 (-73.04, 48.80)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	11 (100.00)	3 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (9.09)	0 (0.00)
		Non-Responders [1]	3 (27.27)	1 (33.33)
		Responders	8 (72.73)	2 (66.67)
		OR (95% CI)	1.33 (0.09, 20.71)	
		RR (95% CI)	1.09 (0.45, 2.63)	
		RD % (95% CI)	6.06 (-53.42, 65.54)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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Composite clinical outcomes responders - improvement in at least 1 of the 3 component assessments by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	7 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	3 (42.86)	5 (83.33)
		Responders	4 (57.14)	1 (16.67)
		OR (95% CI)	6.67 (0.49, 91.33)	
		RR (95% CI)	3.43 (0.51, 22.94)	
		RD % (95% CI)	40.48 (-6.78, 87.73)	
		p-value – Fisher's Exact Test	0.2657	
	Week 24	n (%)	7 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	4 (57.14)	4 (66.67)
		Responders	3 (42.86)	2 (33.33)
		OR (95% CI)	1.50 (0.16, 14.42)	
		RR (95% CI)	1.29 (0.31, 5.31)	
		RD % (95% CI)	9.52 (-43.08, 62.12)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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4.10.5.3 Composite clinical outcomes responders - improvement in at least 1 of the 3 component assessments by region

Region	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
All	Interaction	Treatment*Region, p-value Chi-Square[1]	0.6684	
US	Week 12	n (%)	7 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	3 (42.86)	2 (40.00)
		Responders	4 (57.14)	3 (60.00)
		OR (95% CI)	0.89 (0.09, 9.16)	
		RR (95% CI)	0.95 (0.36, 2.49)	
		RD % (95% CI)	-2.86 (-59.32, 53.60)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	7 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	2 (28.57)	2 (40.00)
		Responders	5 (71.43)	3 (60.00)
		OR (95% CI)	1.67 (0.15, 18.87)	
		RR (95% CI)	1.19 (0.51, 2.80)	
		RD % (95% CI)	11.43 (-43.01, 65.87)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Composite clinical outcomes responders - improvement in at least 1 of the 3 component assessments by region

Region	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
Non-US	Week 12	n (%)	11 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (18.18)	0 (0.00)
		Non-Responders [1]	5 (45.45)	4 (100.00)
		Responders	6 (54.55)	0 (0.00)
		OR (95% CI)	10.64 (0.46, 244.43)	
		RR (95% CI)	5.42 (0.37, 79.05)	
		RD % (95% CI)	44.17 (5.62, 82.72)	
		p-value – Fisher's Exact Test	0.1033	
	Week 24	n (%)	11 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (9.09)	0 (0.00)
		Non-Responders [1]	5 (45.45)	3 (75.00)
		Responders	6 (54.55)	1 (25.00)
		OR (95% CI)	3.60 (0.28, 46.36)	
		RR (95% CI)	2.18 (0.37, 12.95)	
		RD % (95% CI)	29.55 (-22.09, 81.18)	
		p-value – Fisher's Exact Test	0.5692	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.5.4 Composite clinical outcomes responders - improvement in at least 1 of the 3 component assessments by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
All	Interaction	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.5987	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	5 (55.56)	4 (80.00)
		Responders	4 (44.44)	1 (20.00)
		OR (95% CI)	3.20 (0.25, 41.21)	
		RR (95% CI)	2.22 (0.33, 14.84)	
		RD % (95% CI)	24.44 (-23.34, 72.23)	
		p-value – Fisher's Exact Test	0.5804	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	5 (55.56)	4 (80.00)
		Responders	4 (44.44)	1 (20.00)
		OR (95% CI)	3.20 (0.25, 41.21)	
		RR (95% CI)	2.22 (0.33, 14.84)	
		RD % (95% CI)	24.44 (-23.34, 72.23)	
		p-value – Fisher's Exact Test	0.5804	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Composite clinical outcomes responders - improvement in at least 1 of the 3 component assessments by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
≥ II	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	3 (33.33)	2 (50.00)
		Responders	6 (66.67)	2 (50.00)
		OR (95% CI)	2.00 (0.18, 22.06)	
		RR (95% CI)	1.33 (0.45, 3.94)	
		RD % (95% CI)	16.67 (-41.21, 74.54)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	2 (22.22)	1 (25.00)
		Responders	7 (77.78)	3 (75.00)
		OR (95% CI)	1.17 (0.07, 18.35)	
		RR (95% CI)	1.04 (0.53, 2.02)	
		RD % (95% CI)	2.78 (-47.60, 53.16)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.5.5 Composite clinical outcomes responders - improvement in at least 1 of the 3 component assessments with no worsening in any other components by gender

Gender	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
All	Interaction	Treatment*Gender, p-value Chi-Square[1]	0.7392	
Male	Week 12	n (%)	10 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (20.00)	0 (0.00)
		Non-Responders [1]	6 (60.00)	4 (66.67)
		Responders	4 (40.00)	2 (33.33)
		OR (95% CI)	1.33 (0.16, 11.07)	
		RR (95% CI)	1.20 (0.31, 4.69)	
		RD % (95% CI)	6.67 (-41.76, 55.09)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	10 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (10.00)	0 (0.00)
		Non-Responders [1]	6 (60.00)	3 (50.00)
		Responders	4 (40.00)	3 (50.00)
		OR (95% CI)	0.67 (0.09, 5.13)	
		RR (95% CI)	0.80 (0.27, 2.41)	
		RD % (95% CI)	-10.00 (-60.23, 40.23)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Composite clinical outcomes responders - improvement in at least 1 of the 3 component assessments with no worsening in any other components by gender

Gender	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
Female	Week 12	n (%)	8 (100.00)	3 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	4 (50.00)	2 (66.67)
		Responders	4 (50.00)	1 (33.33)
		OR (95% CI)	2.00 (0.13, 31.98)	
		RR (95% CI)	1.50 (0.26, 8.58)	
		RD % (95% CI)	16.67 (-46.94, 80.27)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	8 (100.00)	3 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	5 (62.50)	2 (66.67)
		Responders	3 (37.50)	1 (33.33)
		OR (95% CI)	1.20 (0.07, 19.63)	
		RR (95% CI)	1.13 (0.18, 7.04)	
		RD % (95% CI)	4.17 (-58.85, 67.18)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.5.6 Composite clinical outcomes responders - improvement in at least 1 of the 3 component assessments with no worsening in any other components by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
All	Interaction	Treatment*Age Group, p-value Chi-Square[1]	0.7201	
<10.5 years old at screening	Week 12	n (%)	11 (100.00)	3 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (18.18)	0 (0.00)
		Non-Responders [1]	7 (63.64)	1 (33.33)
		Responders	4 (36.36)	2 (66.67)
		OR (95% CI)	0.29 (0.02, 4.24)	
		RR (95% CI)	0.55 (0.18, 1.67)	
		RD % (95% CI)	-30.30 (-90.75, 30.14)	
		p-value – Fisher's Exact Test	0.5385	
	Week 24	n (%)	11 (100.00)	3 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (9.09)	0 (0.00)
		Non-Responders [1]	6 (54.55)	1 (33.33)
		Responders	5 (45.45)	2 (66.67)
		OR (95% CI)	0.42 (0.03, 6.06)	
		RR (95% CI)	0.68 (0.24, 1.91)	
		RD % (95% CI)	-21.21 (-82.13, 39.71)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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Composite clinical outcomes responders - improvement in at least 1 of the 3 component assessments with no worsening in any other components by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	7 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	3 (42.86)	5 (83.33)
		Responders	4 (57.14)	1 (16.67)
		OR (95% CI)	6.67 (0.49, 91.33)	
		RR (95% CI)	3.43 (0.51, 22.94)	
		RD % (95% CI)	40.48 (-6.78, 87.73)	
		p-value – Fisher's Exact Test	0.2657	
	Week 24	n (%)	7 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	5 (71.43)	4 (66.67)
		Responders	2 (28.57)	2 (33.33)
		OR (95% CI)	0.80 (0.08, 8.47)	
		RR (95% CI)	0.86 (0.17, 4.37)	
		RD % (95% CI)	-4.76 (-55.19, 45.66)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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4.10.5.7 Composite clinical outcomes responders - improvement in at least 1 of the 3 component assessments with no worsening in any other components by region

Region	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
All	Interaction	Treatment*Region, p-value Chi-Square[1]	0.8954	
US	Week 12	n (%)	7 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	3 (42.86)	2 (40.00)
		Responders	4 (57.14)	3 (60.00)
		OR (95% CI)	0.89 (0.09, 9.16)	
		RR (95% CI)	0.95 (0.36, 2.49)	
		RD % (95% CI)	-2.86 (-59.32, 53.60)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	7 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	3 (42.86)	2 (40.00)
		Responders	4 (57.14)	3 (60.00)
		OR (95% CI)	0.89 (0.09, 9.16)	
		RR (95% CI)	0.95 (0.36, 2.49)	
		RD % (95% CI)	-2.86 (-59.32, 53.60)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Composite clinical outcomes responders - improvement in at least 1 of the 3 component assessments with no worsening in any other components by region

Region	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
Non-US	Week 12	n (%)	11 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (18.18)	0 (0.00)
		Non-Responders [1]	7 (63.64)	4 (100.00)
		Responders	4 (36.36)	0 (0.00)
		OR (95% CI)	5.40 (0.23, 125.61)	
		RR (95% CI)	3.75 (0.24, 57.45)	
		RD % (95% CI)	27.50 (-10.47, 65.47)	
		p-value – Fisher's Exact Test	0.5165	
	Week 24	n (%)	11 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (9.09)	0 (0.00)
		Non-Responders [1]	8 (72.73)	3 (75.00)
		Responders	3 (27.27)	1 (25.00)
		OR (95% CI)	1.13 (0.08, 15.51)	
		RR (95% CI)	1.09 (0.15, 7.69)	
		RD % (95% CI)	2.27 (-47.66, 52.21)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.5.8 Composite clinical outcomes responders - improvement in at least 1 of the 3 component assessments with no worsening in any other components by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
All	Interaction	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.1160	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	5 (55.56)	4 (80.00)
		Responders	4 (44.44)	1 (20.00)
		OR (95% CI)	3.20 (0.25, 41.21)	
		RR (95% CI)	2.22 (0.33, 14.84)	
		RD % (95% CI)	24.44 (-23.34, 72.23)	
		p-value – Fisher's Exact Test	0.5804	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	5 (55.56)	4 (80.00)
		Responders	4 (44.44)	1 (20.00)
		OR (95% CI)	3.20 (0.25, 41.21)	
		RR (95% CI)	2.22 (0.33, 14.84)	
		RD % (95% CI)	24.44 (-23.34, 72.23)	
		p-value – Fisher's Exact Test	0.5804	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Composite clinical outcomes responders - improvement in at least 1 of the 3 component assessments with no worsening in any other components by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 18) n (%)	Placebo (N = 9) n (%)
≥ II	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	5 (55.56)	2 (50.00)
		Responders	4 (44.44)	2 (50.00)
		OR (95% CI)	0.80 (0.08, 8.47)	
		RR (95% CI)	0.89 (0.26, 3.02)	
		RD % (95% CI)	-5.56 (-64.33, 53.22)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	6 (66.67)	1 (25.00)
		Responders	3 (33.33)	3 (75.00)
		OR (95% CI)	0.17 (0.01, 2.37)	
		RR (95% CI)	0.44 (0.15, 1.31)	
		RD % (95% CI)	-41.67 (-94.10, 10.77)	
		p-value – Fisher's Exact Test	0.2657	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.6 Subgruppenanalysen für den Endpunkt FMS

4.10.6.1 FMS-5

4.10.6.1.1 FMS-5 by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.5570	
Male	Baseline	Absolute value	n (%)	11 (91.67)	7 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	5.18 (1.250)	4.71 (1.704)
	Week 12	Absolute value	n (%)	10 (83.33)	7 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	5.20 (1.229)	4.86 (1.773)
		Change from Baseline	n (%)	10 (83.33)	7 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.11 (0.159)	0.13 (0.192)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.02 (0.251)	
			95% CI for LS Mean Difference [2]	-0.55, 0.52	
			p-value MMRM [2]	0.9400	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.03	
			95% CI for SMD (Hedges' g)	-1.00, 0.93	
			p-value WRS[3]	1.0000	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.
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1.4.6 FMS
FMS-5 by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	11 (91.67)	7 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	5.09 (1.221)	4.57 (1.902)
		Change from Baseline	n (%)	11 (91.67)	7 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-0.08 (0.185)	-0.16 (0.232)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.07 (0.298)	
			95% CI for LS Mean Difference [2]	-0.56, 0.71	
			p-value MMRM [2]	0.8063	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.11	
			95% CI for SMD (Hedges' g)	-0.84, 1.06	
			p-value WRS[3]	1.0000	
Female	Baseline	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	5.11 (1.616)	5.00 (2.000)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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1.4.6 FMS
FMS-5 by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	5.88 (0.354)	5.00 (2.000)
		Change from Baseline	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.22 (0.206)	-0.00 (0.298)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.22 (0.362)	
			95% CI for LS Mean Difference [2]	-0.58, 1.03	
			p-value MMRM [2]	0.5511	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.34	
			95% CI for SMD (Hedges' g)	-0.87, 1.54	
			p-value WRS[3]	0.4424	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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FMS-5 by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	5.33 (1.658)	5.00 (2.000)
		Change from Baseline	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.22 (0.132)	-0.00 (0.198)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.22 (0.237)	
			95% CI for LS Mean Difference [2]	-0.31, 0.75	
			p-value MMRM [2]	0.3690	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.50	
			95% CI for SMD (Hedges' g)	-0.70, 1.69	
			p-value WRS[3]	0.5385	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.6.1.2 FMS-5 by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.4642	
<10.5 years old at screening	Baseline	Absolute value	n (%)	11 (91.67)	4 (100.00)

		Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
		Mean (SD)	5.36 (1.206)	4.50 (1.732)
Week 12	Absolute value	n (%)	10 (83.33)	4 (100.00)
		Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
		Mean (SD)	5.40 (1.265)	4.75 (1.893)
	Change from Baseline	n (%)	10 (83.33)	4 (100.00)
		Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
		LS Mean Change from Baseline (SE) [2]	0.08 (0.171)	0.25 (0.282)
		LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.17 (0.334)	
		95% CI for LS Mean Difference [2]	-0.89, 0.56	
		p-value MMRM [2]	0.6267	
		SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.28	
		95% CI for SMD (Hedges' g)	-1.44, 0.89	
		p-value WRS[3]	1.0000	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

NOTE: Median age used as cut-off point.

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FMS-5 by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	5.55 (1.214)	4.75 (1.893)
		Change from Baseline	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.18 (0.137)	0.25 (0.230)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.07 (0.274)	
			95% CI for LS Mean Difference [2]	-0.66, 0.53	
			p-value MMRM [2]	0.8156	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.13	
			95% CI for SMD (Hedges' g)	-1.27, 1.02	
			p-value WRS[3]	1.0000	
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	4.89 (1.616)	5.00 (1.826)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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FMS-5 by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	8 (88.89)	7 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	5.63 (0.518)	5.00 (1.826)
		Change from Baseline	n (%)	8 (88.89)	7 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.26 (0.181)	-0.00 (0.192)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.27 (0.264)	
			95% CI for LS Mean Difference [2]	-0.30, 0.84	
			p-value MMRM [2]	0.3272	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.48	
			95% CI for SMD (Hedges' g)	-0.55, 1.51	
			p-value WRS[3]	0.4154	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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FMS-5 by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	4.78 (1.563)	4.71 (1.976)
		Change from Baseline	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-0.12 (0.191)	-0.29 (0.216)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.17 (0.288)	
			95% CI for LS Mean Difference [2]	-0.45, 0.79	
			p-value MMRM [2]	0.5707	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.27	
			95% CI for SMD (Hedges' g)	-0.73, 1.26	
			p-value WRS[3]	0.7375	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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4.10.6.1.3 FMS-5 by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.1519	
US	Baseline	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	5.63 (0.744)	4.83 (1.941)
	Week 12	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	5.63 (0.518)	5.00 (2.000)
		Change from Baseline	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.01 (0.229)	0.15 (0.266)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.13 (0.357)	
			95% CI for LS Mean Difference [2]	-0.92, 0.65	
			p-value MMRM [2]	0.7124	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.19	
			95% CI for SMD (Hedges' g)	-1.25, 0.88	
			p-value WRS[3]	0.7123	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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FMS-5 by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	5.63 (0.744)	5.00 (2.000)
		Change from Baseline	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.01 (0.183)	0.15 (0.213)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.13 (0.287)	
			95% CI for LS Mean Difference [2]	-0.77, 0.50	
			p-value MMRM [2]	0.6482	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.23	
			95% CI for SMD (Hedges' g)	-1.29, 0.83	
			p-value WRS[3]	0.6264	
Non-US	Baseline	Absolute value	n (%)	12 (92.31)	5 (100.00)
			Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
			Mean (SD)	4.83 (1.642)	4.80 (1.643)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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FMS-5 by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	10 (76.92)	5 (100.00)
			Number of patients with missing data: n (%)	3 (23.08)	0 (0.00)
			Mean (SD)	5.40 (1.265)	4.80 (1.643)
		Change from Baseline	n (%)	10 (76.92)	5 (100.00)
			Number of patients with missing data: n (%)	3 (23.08)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.30 (0.131)	-0.00 (0.183)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.30 (0.225)	
			95% CI for LS Mean Difference [2]	-0.19, 0.79	
			p-value MMRM [2]	0.2077	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.66	
			95% CI for SMD (Hedges' g)	-0.44, 1.76	
			p-value WRS[3]	0.5055	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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FMS-5 by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	12 (92.31)	5 (100.00)
			Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
			Mean (SD)	4.92 (1.676)	4.40 (1.817)
		Change from Baseline	n (%)	12 (92.31)	5 (100.00)
			Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.08 (0.154)	-0.40 (0.239)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.48 (0.284)	
			95% CI for LS Mean Difference [2]	-0.12, 1.09	
			p-value MMRM [2]	0.1103	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.83	
			95% CI for SMD (Hedges' g)	-0.25, 1.91	
			p-value WRS[3]	0.4412	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.6.1.4 FMS-5 by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.2854	
I	Baseline	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	6.00 (0.000)	6.00 (0.000)
	Week 12	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	5.88 (0.354)	6.00 (0.000)
		Change from Baseline	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			p-value WRS[3]	1.0000	
	Week 24	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	5.88 (0.354)	6.00 (0.000)
		Change from Baseline	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			p-value WRS[3]	1.0000	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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FMS-5 by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Baseline	Absolute value	n (%)	12 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	4.58 (1.564)	3.83 (1.835)
	Week 12	Absolute value	n (%)	10 (83.33)	6 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	5.20 (1.229)	4.00 (2.000)
		Change from Baseline	n (%)	10 (83.33)	6 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.39 (0.202)	0.17 (0.264)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.22 (0.337)	
			95% CI for LS Mean Difference [2]	-0.47, 0.91	
			p-value MMRM [2]	0.5157	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.33	
			95% CI for SMD (Hedges' g)	-0.69, 1.35	
			p-value WRS[3]	0.5167	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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FMS-5 by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	12 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	4.75 (1.658)	3.67 (1.966)
		Change from Baseline	n (%)	12 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.17 (0.185)	-0.17 (0.264)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.34 (0.325)	
			95% CI for LS Mean Difference [2]	-0.33, 1.00	
			p-value MMRM [2]	0.3119	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.50	
			95% CI for SMD (Hedges' g)	-0.50, 1.49	
			p-value WRS[3]	0.6176	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.6.1.5 FMS-5 responders ≥ 1 level by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Gender, p-value Chi-Square[1]	0.9677	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	9 (75.00)	6 (85.71)
		Responders	3 (25.00)	1 (14.29)
		OR (95% CI)	2.00 (0.17, 24.07)	
		RR (95% CI)	1.75 (0.22, 13.76)	
		RD % (95% CI)	10.71 (-24.95, 46.38)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [2]	11 (91.67)	5 (71.43)
		Responders	1 (8.33)	2 (28.57)
		OR (95% CI)	0.23 (0.02, 3.13)	
		RR (95% CI)	0.29 (0.03, 2.66)	
		RD % (95% CI)	-20.24 (-57.18, 16.70)	
		p-value – Fisher's Exact Test	0.5232	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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FMS-5 responders ≥ 1 level by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	5 (55.56)	4 (100.00)
		Responders	4 (44.44)	0 (0.00)
		OR (95% CI)	7.36 (0.31, 176.41)	
		RR (95% CI)	4.50 (0.30, 68.13)	
		RD % (95% CI)	35.00 (-5.52, 75.52)	
		p-value – Fisher's Exact Test	0.2280	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	7 (77.78)	4 (100.00)
		Responders	2 (22.22)	0 (0.00)
		OR (95% CI)	3.00 (0.12, 77.64)	
		RR (95% CI)	2.50 (0.15, 42.80)	
		RD % (95% CI)	15.00 (-22.57, 52.57)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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4.10.6.1.6 FMS-5 responders ≥ 1 level by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Age Group, p-value Chi-Square[1]	0.9135	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	9 (75.00)	3 (75.00)
		Responders	3 (25.00)	1 (25.00)
		OR (95% CI)	1.00 (0.07, 13.64)	
		RR (95% CI)	1.00 (0.14, 7.10)	
		RD % (95% CI)	0.00 (-49.00, 49.00)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [2]	10 (83.33)	3 (75.00)
		Responders	2 (16.67)	1 (25.00)
		OR (95% CI)	0.60 (0.04, 9.16)	
		RR (95% CI)	0.67 (0.08, 5.54)	
		RD % (95% CI)	-8.33 (-55.72, 39.05)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
Program: t-qs-categ-sub.sas
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FMS-5 responders ≥ 1 level by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	5 (55.56)	7 (100.00)
		Responders	4 (44.44)	0 (0.00)
		OR (95% CI)	12.27 (0.54, 278.50)	
		RR (95% CI)	7.20 (0.45, 114.89)	
		RD % (95% CI)	38.75 (3.65, 73.85)	
		p-value – Fisher's Exact Test	0.0885	
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	8 (88.89)	6 (85.71)
		Responders	1 (11.11)	1 (14.29)
		OR (95% CI)	0.75 (0.04, 14.58)	
		RR (95% CI)	0.78 (0.06, 10.37)	
		RD % (95% CI)	-3.17 (-36.24, 29.89)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
Program: t-qs-categ-sub.sas
Table Generation: 11SEP2023 12:19:05 PM

4.10.6.1.7 FMS-5 responders ≥ 1 level by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Region, p-value Chi-Square[1]	0.4323	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	4 (50.00)	5 (83.33)
		Responders	4 (50.00)	1 (16.67)
		OR (95% CI)	5.00 (0.39, 64.39)	
		RR (95% CI)	3.00 (0.44, 20.44)	
		RD % (95% CI)	33.33 (-12.38, 79.05)	
		p-value – Fisher's Exact Test	0.3007	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	6 (75.00)	5 (83.33)
		Responders	2 (25.00)	1 (16.67)
		OR (95% CI)	1.67 (0.11, 24.26)	
		RR (95% CI)	1.50 (0.17, 12.94)	
		RD % (95% CI)	8.33 (-33.97, 50.64)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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FMS-5 responders ≥ 1 level by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (23.08)	0 (0.00)
		Non-Responders [2]	10 (76.92)	5 (100.00)
		Responders	3 (23.08)	0 (0.00)
		OR (95% CI)	3.67 (0.16, 84.51)	
		RR (95% CI)	3.00 (0.18, 49.56)	
		RD % (95% CI)	16.67 (-15.01, 48.35)	
		p-value – Fisher's Exact Test	0.5221	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (7.69)	0 (0.00)
		Non-Responders [2]	12 (92.31)	4 (80.00)
		Responders	1 (7.69)	1 (20.00)
		OR (95% CI)	0.33 (0.02, 6.65)	
		RR (95% CI)	0.38 (0.03, 5.04)	
		RD % (95% CI)	-12.31 (-50.24, 25.63)	
		p-value – Fisher's Exact Test	0.4902	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.6.1.8 FMS-5 responders ≥ 1 level by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.9677	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	8 (88.89)	5 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	1.94 (0.07, 56.76)	
		RR (95% CI)	1.80 (0.09, 37.49)	
		RD % (95% CI)	6.67 (-24.62, 37.95)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	8 (88.89)	5 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	1.94 (0.07, 56.76)	
		RR (95% CI)	1.80 (0.09, 37.49)	
		RD % (95% CI)	6.67 (-24.62, 37.95)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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FMS-5 responders ≥ 1 level by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	6 (50.00)	5 (83.33)
		Responders	6 (50.00)	1 (16.67)
		OR (95% CI)	5.00 (0.44, 56.62)	
		RR (95% CI)	3.00 (0.46, 19.59)	
		RD % (95% CI)	33.33 (-7.77, 74.44)	
		p-value – Fisher's Exact Test	0.3156	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	10 (83.33)	4 (66.67)
		Responders	2 (16.67)	2 (33.33)
		OR (95% CI)	0.40 (0.04, 3.90)	
		RR (95% CI)	0.50 (0.09, 2.73)	
		RD % (95% CI)	-16.67 (-59.88, 26.55)	
		p-value – Fisher's Exact Test	0.5686	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.6.2 FMS-50

4.10.6.2.1 FMS-50 by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.4401	
Male	Baseline	Absolute value	n (%)	10 (83.33)	7 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	5.00 (1.491)	4.57 (1.618)
	Week 12	Absolute value	n (%)	10 (83.33)	7 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	4.80 (1.814)	4.29 (1.976)
		Change from Baseline	n (%)	9 (75.00)	7 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.13 (0.293)	-0.29 (0.331)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.42 (0.443)	
			95% CI for LS Mean Difference [2]	-0.53, 1.37	
			p-value MMRM [2]	0.3578	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.44	
			95% CI for SMD (Hedges' g)	-0.56, 1.44	
			p-value WRS[3]	1.0000	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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FMS-50 by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	11 (91.67)	7 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	5.00 (1.483)	4.57 (1.902)
		Change from Baseline	n (%)	10 (83.33)	7 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.10 (0.221)	-0.00 (0.264)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.10 (0.345)	
			95% CI for LS Mean Difference [2]	-0.63, 0.84	
			p-value MMRM [2]	0.7681	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.14	
			95% CI for SMD (Hedges' g)	-0.83, 1.10	
			p-value WRS[3]	0.7353	
Female	Baseline	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	5.00 (1.581)	4.50 (2.380)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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FMS-50 by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	5.57 (0.535)	5.00 (2.000)
		Change from Baseline	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-0.02 (0.205)	0.45 (0.272)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.47 (0.344)	
			95% CI for LS Mean Difference [2]	-1.25, 0.31	
			p-value MMRM [2]	0.2057	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.75	
			95% CI for SMD (Hedges' g)	-2.02, 0.53	
			p-value WRS[3]	0.3212	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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FMS-50 by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	5.33 (1.658)	4.75 (1.893)
		Change from Baseline	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.33 (0.163)	0.20 (0.248)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.13 (0.297)	
			95% CI for LS Mean Difference [2]	-0.53, 0.79	
			p-value MMRM [2]	0.6621	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.24	
			95% CI for SMD (Hedges' g)	-0.94, 1.42	
			p-value WRS[3]	1.0000	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.6.2.2 FMS-50 by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.2763	
<10.5 years old at screening	Baseline	Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	5.09 (1.446)	4.00 (2.000)
	Week 12	Absolute value	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	5.10 (1.524)	3.75 (2.062)
		Change from Baseline	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.09 (0.326)	-0.27 (0.526)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.36 (0.622)	
			95% CI for LS Mean Difference [2]	-1.00, 1.72	
			p-value MMRM [2]	0.5746	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.31	
			95% CI for SMD (Hedges' g)	-0.85, 1.48	
			p-value WRS[3]	0.6553	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

NOTE: Median age used as cut-off point.

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FMS-50 by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	5.45 (1.508)	4.75 (1.893)
		Change from Baseline	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.37 (0.159)	0.73 (0.271)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.36 (0.321)	
			95% CI for LS Mean Difference [2]	-1.06, 0.34	
			p-value MMRM [2]	0.2886	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.60	
			95% CI for SMD (Hedges' g)	-1.77, 0.56	
			p-value WRS[3]	0.2821	
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	8 (88.89)	7 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	4.88 (1.642)	4.86 (1.773)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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FMS-50 by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	7 (77.78)	7 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	5.14 (1.464)	5.00 (1.826)
		Change from Baseline	n (%)	6 (66.67)	7 (100.00)
			Number of patients with missing data: n (%)	3 (33.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.17 (0.169)	0.14 (0.152)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.03 (0.229)	
			95% CI for LS Mean Difference [2]	-0.47, 0.53	
			p-value MMRM [2]	0.8954	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.07	
			95% CI for SMD (Hedges' g)	-1.02, 1.16	
			p-value WRS[3]	1.0000	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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FMS-50 by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	4.78 (1.563)	4.57 (1.902)
		Change from Baseline	n (%)	8 (88.89)	7 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-0.00 (0.186)	-0.29 (0.199)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.29 (0.272)	
			95% CI for LS Mean Difference [2]	-0.30, 0.87	
			p-value MMRM [2]	0.3124	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.49	
			95% CI for SMD (Hedges' g)	-0.54, 1.52	
			p-value WRS[3]	0.4667	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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4.10.6.2.3 FMS-50 by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.4081	
US	Baseline	Absolute value	n (%)	7 (87.50)	6 (100.00)
			Number of patients with missing data: n (%)	1 (12.50)	0 (0.00)
			Mean (SD)	5.71 (0.488)	4.50 (1.761)
	Week 12	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	5.13 (1.356)	4.33 (2.251)
		Change from Baseline	n (%)	7 (87.50)	6 (100.00)
			Number of patients with missing data: n (%)	1 (12.50)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-0.15 (0.400)	-0.16 (0.433)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.01 (0.598)	
			95% CI for LS Mean Difference [2]	-1.30, 1.31	
			p-value MMRM [2]	0.9892	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.01	
			95% CI for SMD (Hedges' g)	-1.08, 1.10	
			p-value WRS[3]	0.6364	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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FMS-50 by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	5.63 (0.744)	4.83 (1.941)
		Change from Baseline	n (%)	7 (87.50)	6 (100.00)
			Number of patients with missing data: n (%)	1 (12.50)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.14 (0.189)	0.34 (0.207)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.21 (0.299)	
			95% CI for LS Mean Difference [2]	-0.87, 0.46	
			p-value MMRM [2]	0.5067	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.36	
			95% CI for SMD (Hedges' g)	-1.46, 0.74	
			p-value WRS[3]	0.5594	
Non-US	Baseline	Absolute value	n (%)	12 (92.31)	5 (100.00)
			Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
			Mean (SD)	4.58 (1.730)	4.60 (2.074)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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FMS-50 by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	9 (69.23)	5 (100.00)
			Number of patients with missing data: n (%)	4 (30.77)	0 (0.00)
			Mean (SD)	5.11 (1.616)	4.80 (1.643)
		Change from Baseline	n (%)	9 (69.23)	5 (100.00)
			Number of patients with missing data: n (%)	4 (30.77)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.24 (0.142)	0.19 (0.190)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.05 (0.238)	
			95% CI for LS Mean Difference [2]	-0.47, 0.56	
			p-value MMRM [2]	0.8521	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.10	
			95% CI for SMD (Hedges' g)	-1.00, 1.19	
			p-value WRS[3]	1.0000	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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FMS-50 by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	12 (92.31)	5 (100.00)
			Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
			Mean (SD)	4.83 (1.850)	4.40 (1.817)
		Change from Baseline	n (%)	12 (92.31)	5 (100.00)
			Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.24 (0.198)	-0.21 (0.307)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.45 (0.365)	
			95% CI for LS Mean Difference [2]	-0.33, 1.23	
			p-value MMRM [2]	0.2387	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.60	
			95% CI for SMD (Hedges' g)	-0.47, 1.67	
			p-value WRS[3]	0.6160	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.6.2.4 FMS-50 by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.2788	
I	Baseline	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	5.75 (0.463)	5.60 (0.548)
	Week 12	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	5.75 (0.463)	5.80 (0.447)
		Change from Baseline	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.02 (0.091)	0.17 (0.115)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.15 (0.147)	
			95% CI for LS Mean Difference [2]	-0.47, 0.18	
			p-value MMRM [2]	0.3336	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.51	
			95% CI for SMD (Hedges' g)	-1.65, 0.62	
			p-value WRS[3]	0.3846	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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FMS-50 by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	5.88 (0.354)	5.80 (0.447)
		Change from Baseline	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.14 (0.111)	0.17 (0.140)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.02 (0.179)	
			95% CI for LS Mean Difference [2]	-0.42, 0.37	
			p-value MMRM [2]	0.8983	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.07	
			95% CI for SMD (Hedges' g)	-1.18, 1.05	
			p-value WRS[3]	1.0000	
≥ II	Baseline	Absolute value	n (%)	11 (91.67)	6 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	4.45 (1.753)	3.67 (2.066)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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FMS-50 by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	9 (75.00)	6 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			Mean (SD)	4.56 (1.810)	3.50 (2.074)
		Change from Baseline	n (%)	8 (66.67)	6 (100.00)
			Number of patients with missing data: n (%)	4 (33.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.16 (0.380)	-0.20 (0.434)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.37 (0.582)	
			95% CI for LS Mean Difference [2]	-0.90, 1.63	
			p-value MMRM [2]	0.5411	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.31	
			95% CI for SMD (Hedges' g)	-0.76, 1.37	
			p-value WRS[3]	0.9254	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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FMS-50 by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	12 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	4.67 (1.826)	3.67 (1.966)
		Change from Baseline	n (%)	11 (91.67)	6 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.29 (0.229)	-0.04 (0.314)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.33 (0.393)	
			95% CI for LS Mean Difference [2]	-0.51, 1.17	
			p-value MMRM [2]	0.4204	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.39	
			95% CI for SMD (Hedges' g)	-0.61, 1.39	
			p-value WRS[3]	1.0000	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.6.2.5 FMS-50 responders ≥ 1 level by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Gender, p-value Chi-Square[1]	0.1792	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (25.00)	0 (0.00)
		Non-Responders [2]	11 (91.67)	5 (71.43)
		Responders	1 (8.33)	2 (28.57)
		OR (95% CI)	0.23 (0.02, 3.13)	
		RR (95% CI)	0.29 (0.03, 2.66)	
		RD % (95% CI)	-20.24 (-57.18, 16.70)	
		p-value – Fisher's Exact Test	0.5232	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	11 (91.67)	4 (57.14)
		Responders	1 (8.33)	3 (42.86)
		OR (95% CI)	0.12 (0.01, 1.53)	
		RR (95% CI)	0.19 (0.02, 1.53)	
		RD % (95% CI)	-34.52 (-74.38, 5.33)	
		p-value – Fisher's Exact Test	0.1174	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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FMS-50 responders ≥ 1 level by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (22.22)	0 (0.00)
		Non-Responders [2]	7 (77.78)	2 (50.00)
		Responders	2 (22.22)	2 (50.00)
		OR (95% CI)	0.29 (0.02, 3.52)	
		RR (95% CI)	0.44 (0.09, 2.13)	
		RD % (95% CI)	-27.78 (-83.80, 28.25)	
		p-value – Fisher's Exact Test	0.5301	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	6 (66.67)	3 (75.00)
		Responders	3 (33.33)	1 (25.00)
		OR (95% CI)	1.50 (0.11, 21.31)	
		RR (95% CI)	1.33 (0.19, 9.21)	
		RD % (95% CI)	8.33 (-44.10, 60.77)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.6.2.6 FMS-50 responders ≥ 1 level by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Age Group, p-value Chi-Square[1]	0.9729	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	10 (83.33)	1 (25.00)
		Responders	2 (16.67)	3 (75.00)
		OR (95% CI)	0.07 (0.00, 1.02)	
		RR (95% CI)	0.22 (0.06, 0.89)	
		RD % (95% CI)	-58.33 (-100.00, -10.95)	
		p-value – Fisher's Exact Test	0.0632	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [2]	8 (66.67)	1 (25.00)
		Responders	4 (33.33)	3 (75.00)
		OR (95% CI)	0.17 (0.01, 2.16)	
		RR (95% CI)	0.44 (0.17, 1.18)	
		RD % (95% CI)	-41.67 (-91.79, 8.45)	
		p-value – Fisher's Exact Test	0.2615	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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FMS-50 responders ≥ 1 level by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (33.33)	0 (0.00)
		Non-Responders [2]	8 (88.89)	6 (85.71)
		Responders	1 (11.11)	1 (14.29)
		OR (95% CI)	0.75 (0.04, 14.58)	
		RR (95% CI)	0.78 (0.06, 10.37)	
		RD % (95% CI)	-3.17 (-36.24, 29.89)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	9 (100.00)	6 (85.71)
		Responders	0 (0.00)	1 (14.29)
		OR (95% CI)	0.23 (0.01, 6.52)	
		RR (95% CI)	0.27 (0.01, 5.70)	
		RD % (95% CI)	-13.75 (-43.98, 16.48)	
		p-value – Fisher's Exact Test	0.4375	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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4.10.6.2.7 FMS-50 responders ≥ 1 level by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Region, p-value Chi-Square[1]	0.7983	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (12.50)	0 (0.00)
		Non-Responders [2]	7 (87.50)	3 (50.00)
		Responders	1 (12.50)	3 (50.00)
		OR (95% CI)	0.14 (0.01, 1.99)	
		RR (95% CI)	0.25 (0.03, 1.85)	
		RD % (95% CI)	-37.50 (-83.61, 8.61)	
		p-value – Fisher's Exact Test	0.2448	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (12.50)	0 (0.00)
		Non-Responders [2]	7 (87.50)	4 (66.67)
		Responders	1 (12.50)	2 (33.33)
		OR (95% CI)	0.29 (0.02, 4.24)	
		RR (95% CI)	0.38 (0.04, 3.23)	
		RD % (95% CI)	-20.83 (-64.97, 23.30)	
		p-value – Fisher's Exact Test	0.5385	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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FMS-50 responders ≥ 1 level by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	4 (30.77)	0 (0.00)
		Non-Responders [2]	11 (84.62)	4 (80.00)
		Responders	2 (15.38)	1 (20.00)
		OR (95% CI)	0.73 (0.05, 10.39)	
		RR (95% CI)	0.77 (0.09, 6.72)	
		RD % (95% CI)	-4.62 (-44.79, 35.56)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (7.69)	0 (0.00)
		Non-Responders [2]	10 (76.92)	3 (60.00)
		Responders	3 (23.08)	2 (40.00)
		OR (95% CI)	0.45 (0.05, 4.09)	
		RR (95% CI)	0.58 (0.13, 2.49)	
		RD % (95% CI)	-16.92 (-65.59, 31.74)	
		p-value – Fisher's Exact Test	0.5827	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.6.2.8 FMS-50 responders ≥ 1 level by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.8280	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	9 (100.00)	4 (80.00)
		Responders	0 (0.00)	1 (20.00)
		OR (95% CI)	0.16 (0.01, 4.69)	
		RR (95% CI)	0.20 (0.01, 4.17)	
		RD % (95% CI)	-20.00 (-57.19, 17.19)	
		p-value – Fisher's Exact Test	0.3571	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	8 (88.89)	4 (80.00)
		Responders	1 (11.11)	1 (20.00)
		OR (95% CI)	0.50 (0.02, 10.25)	
		RR (95% CI)	0.56 (0.04, 7.09)	
		RD % (95% CI)	-8.89 (-49.52, 31.74)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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FMS-50 responders ≥ 1 level by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	4 (33.33)	0 (0.00)
		Non-Responders [2]	9 (75.00)	3 (50.00)
		Responders	3 (25.00)	3 (50.00)
		OR (95% CI)	0.33 (0.04, 2.63)	
		RR (95% CI)	0.50 (0.14, 1.77)	
		RD % (95% CI)	-25.00 (-71.91, 21.91)	
		p-value – Fisher's Exact Test	0.3441	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [2]	9 (75.00)	3 (50.00)
		Responders	3 (25.00)	3 (50.00)
		OR (95% CI)	0.33 (0.04, 2.63)	
		RR (95% CI)	0.50 (0.14, 1.77)	
		RD % (95% CI)	-25.00 (-71.91, 21.91)	
		p-value – Fisher's Exact Test	0.3441	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.6.2.9 FMS-500

4.10.6.2.10 FMS-500 by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.0892	
Male	Baseline	Absolute value	n (%)	10 (83.33)	7 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	4.80 (1.476)	3.29 (2.215)
	Week 12	Absolute value	n (%)	10 (83.33)	7 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	4.50 (1.958)	3.57 (2.440)
		Change from Baseline	n (%)	9 (75.00)	7 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.08 (0.189)	0.33 (0.215)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.25 (0.291)	
			95% CI for LS Mean Difference [2]	-0.87, 0.37	
			p-value MMRM [2]	0.4057	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.40	
			95% CI for SMD (Hedges' g)	-1.40, 0.60	
			p-value WRS[3]	0.7375	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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FMS-500 by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	10 (83.33)	7 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	4.40 (1.897)	3.57 (2.440)
		Change from Baseline	n (%)	9 (75.00)	7 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-0.03 (0.110)	0.33 (0.127)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.36 (0.175)	
			95% CI for LS Mean Difference [2]	-0.74, 0.02	
			p-value MMRM [2]	0.0609	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.98	
			95% CI for SMD (Hedges' g)	-2.03, 0.07	
			p-value WRS[3]	0.1750	
Female	Baseline	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	4.33 (1.936)	4.50 (2.380)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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FMS-500 by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	4.86 (1.773)	4.25 (2.217)
		Change from Baseline	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.11 (0.151)	-0.25 (0.210)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.36 (0.258)	
			95% CI for LS Mean Difference [2]	-0.21, 0.94	
			p-value MMRM [2]	0.1896	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.79	
			95% CI for SMD (Hedges' g)	-0.49, 2.07	
			p-value WRS[3]	0.5091	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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FMS-500 by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	4.44 (2.007)	4.50 (2.380)
		Change from Baseline	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.11 (0.099)	0.00 (0.148)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.11 (0.178)	
			95% CI for LS Mean Difference [2]	-0.28, 0.51	
			p-value MMRM [2]	0.5385	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.34	
			95% CI for SMD (Hedges' g)	-0.85, 1.52	
			p-value WRS[3]	1.0000	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.6.2.11 FMS-500 by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.0531	
<10.5 years old at screening	Baseline	Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	4.55 (1.809)	2.75 (2.062)
	Week 12	Absolute value	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	4.60 (1.955)	3.25 (2.630)
		Change from Baseline	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.06 (0.157)	0.60 (0.256)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.54 (0.309)	
			95% CI for LS Mean Difference [2]	-1.19, 0.12	
			p-value MMRM [2]	0.1038	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.99	
			95% CI for SMD (Hedges' g)	-2.21, 0.24	
			p-value WRS[3]	0.7802	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

NOTE: Median age used as cut-off point.

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FMS-500 by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	4.60 (1.955)	3.25 (2.630)
		Change from Baseline	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.06 (0.157)	0.60 (0.256)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.54 (0.309)	
			95% CI for LS Mean Difference [2]	-1.19, 0.12	
			p-value MMRM [2]	0.1038	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.99	
			95% CI for SMD (Hedges' g)	-2.21, 0.24	
			p-value WRS[3]	0.1758	
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	8 (88.89)	7 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	4.63 (1.598)	4.29 (2.289)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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FMS-500 by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	7 (77.78)	7 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	4.71 (1.799)	4.14 (2.193)
		Change from Baseline	n (%)	6 (66.67)	7 (100.00)
			Number of patients with missing data: n (%)	3 (33.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.18 (0.113)	-0.15 (0.102)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.33 (0.153)	
			95% CI for LS Mean Difference [2]	0.01, 0.65	
			p-value MMRM [2]	0.0421 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.15	
			95% CI for SMD (Hedges' g)	-0.05, 2.34	
			p-value WRS[3]	0.5385	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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FMS-500 by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	4.22 (1.922)	4.29 (2.289)
		Change from Baseline	n (%)	8 (88.89)	7 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.00 (0.095)	-0.01 (0.102)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.01 (0.139)	
			95% CI for LS Mean Difference [2]	-0.28, 0.30	
			p-value MMRM [2]	0.9567	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.03	
			95% CI for SMD (Hedges' g)	-0.99, 1.04	
			p-value WRS[3]	1.0000	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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4.10.6.2.12 FMS-500 by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.4206	
US	Baseline	Absolute value	n (%)	7 (87.50)	6 (100.00)
			Number of patients with missing data: n (%)	1 (12.50)	0 (0.00)
			Mean (SD)	4.86 (1.773)	3.67 (2.160)
	Week 12	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	4.50 (2.204)	4.00 (2.366)
		Change from Baseline	n (%)	7 (87.50)	6 (100.00)
			Number of patients with missing data: n (%)	1 (12.50)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.13 (0.215)	0.35 (0.233)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.23 (0.324)	
			95% CI for LS Mean Difference [2]	-0.93, 0.47	
			p-value MMRM [2]	0.4951	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.36	
			95% CI for SMD (Hedges' g)	-1.46, 0.74	
			p-value WRS[3]	0.7308	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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FMS-500 by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	4.50 (2.204)	4.00 (2.366)
		Change from Baseline	n (%)	7 (87.50)	6 (100.00)
			Number of patients with missing data: n (%)	1 (12.50)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.13 (0.215)	0.35 (0.233)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.23 (0.324)	
			95% CI for LS Mean Difference [2]	-0.93, 0.47	
			p-value MMRM [2]	0.4951	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.36	
			95% CI for SMD (Hedges' g)	-1.46, 0.74	
			p-value WRS[3]	0.5594	
Non-US	Baseline	Absolute value	n (%)	12 (92.31)	5 (100.00)
			Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
			Mean (SD)	4.42 (1.676)	3.80 (2.588)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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FMS-500 by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	9 (69.23)	5 (100.00)
			Number of patients with missing data: n (%)	4 (30.77)	0 (0.00)
			Mean (SD)	4.78 (1.563)	3.60 (2.408)
		Change from Baseline	n (%)	9 (69.23)	5 (100.00)
			Number of patients with missing data: n (%)	4 (30.77)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.12 (0.088)	-0.21 (0.116)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.33 (0.146)	
			95% CI for LS Mean Difference [2]	0.03, 0.63	
			p-value MMRM [2]	0.0344 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.19	
			95% CI for SMD (Hedges' g)	-0.00, 2.38	
			p-value WRS[3]	0.4945	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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FMS-500 by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	11 (84.62)	5 (100.00)
			Number of patients with missing data: n (%)	2 (15.38)	0 (0.00)
			Mean (SD)	4.36 (1.748)	3.80 (2.588)
		Change from Baseline	n (%)	11 (84.62)	5 (100.00)
			Number of patients with missing data: n (%)	2 (15.38)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.00 (0.078)	-0.01 (0.116)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.01 (0.140)	
			95% CI for LS Mean Difference [2]	-0.28, 0.30	
			p-value MMRM [2]	0.9418	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.04	
			95% CI for SMD (Hedges' g)	-1.02, 1.10	
			p-value WRS[3]	1.0000	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.6.2.13 FMS-500 by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.7723	
I	Baseline	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	5.50 (0.535)	5.60 (0.548)
	Week 12	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	5.63 (0.518)	5.40 (0.548)
		Change from Baseline	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.11 (0.132)	-0.18 (0.167)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.29 (0.214)	
			95% CI for LS Mean Difference [2]	-0.18, 0.77	
			p-value MMRM [2]	0.1985	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.69	
			95% CI for SMD (Hedges' g)	-0.46, 1.85	
			p-value WRS[3]	0.5128	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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FMS-500 by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	5.63 (0.518)	5.80 (0.447)
		Change from Baseline	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.11 (0.127)	0.22 (0.160)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.11 (0.205)	
			95% CI for LS Mean Difference [2]	-0.56, 0.35	
			p-value MMRM [2]	0.6137	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.26	
			95% CI for SMD (Hedges' g)	-1.39, 0.86	
			p-value WRS[3]	1.0000	
≥ II	Baseline	Absolute value	n (%)	11 (91.67)	6 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	3.91 (1.921)	2.17 (1.835)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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FMS-500 by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	9 (75.00)	6 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			Mean (SD)	3.78 (2.167)	2.50 (2.345)
		Change from Baseline	n (%)	8 (66.67)	6 (100.00)
			Number of patients with missing data: n (%)	4 (33.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.12 (0.182)	0.35 (0.229)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.23 (0.293)	
			95% CI for LS Mean Difference [2]	-0.85, 0.40	
			p-value MMRM [2]	0.4525	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.39	
			95% CI for SMD (Hedges' g)	-1.46, 0.68	
			p-value WRS[3]	0.7363	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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FMS-500 by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	11 (91.67)	6 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	3.55 (2.067)	2.33 (2.066)
		Change from Baseline	n (%)	10 (83.33)	6 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-0.01 (0.079)	0.18 (0.104)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.19 (0.135)	
			95% CI for LS Mean Difference [2]	-0.48, 0.10	
			p-value MMRM [2]	0.1855	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.68	
			95% CI for SMD (Hedges' g)	-1.72, 0.36	
			p-value WRS[3]	0.3750	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.6.2.14 FMS-500 responders ≥ 1 level by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Gender, p-value Chi-Square[1]	0.9395	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (25.00)	0 (0.00)
		Non-Responders [2]	11 (91.67)	6 (85.71)
		Responders	1 (8.33)	1 (14.29)
		OR (95% CI)	0.55 (0.03, 10.37)	
		RR (95% CI)	0.58 (0.04, 7.94)	
		RD % (95% CI)	-5.95 (-36.23, 24.32)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (25.00)	0 (0.00)
		Non-Responders [2]	12 (100.00)	5 (71.43)
		Responders	0 (0.00)	2 (28.57)
		OR (95% CI)	0.09 (0.00, 2.15)	
		RR (95% CI)	0.12 (0.01, 2.25)	
		RD % (95% CI)	-27.40 (-61.18, 6.37)	
		p-value – Fisher's Exact Test	0.1228	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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FMS-500 responders ≥ 1 level by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (22.22)	0 (0.00)
		Non-Responders [2]	8 (88.89)	3 (75.00)
		Responders	1 (11.11)	1 (25.00)
		OR (95% CI)	0.38 (0.02, 8.10)	
		RR (95% CI)	0.44 (0.04, 5.46)	
		RD % (95% CI)	-13.89 (-61.03, 33.25)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	8 (88.89)	4 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	1.59 (0.05, 47.52)	
		RR (95% CI)	1.50 (0.07, 30.59)	
		RD % (95% CI)	5.00 (-29.37, 39.37)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.6.2.15 FMS-500 responders ≥ 1 level by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Age Group, p-value Chi-Square[1]	0.9945	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	11 (91.67)	3 (75.00)
		Responders	1 (8.33)	1 (25.00)
		OR (95% CI)	0.27 (0.01, 5.77)	
		RR (95% CI)	0.33 (0.03, 4.19)	
		RD % (95% CI)	-16.67 (-61.89, 28.56)	
		p-value – Fisher's Exact Test	0.4500	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	11 (91.67)	2 (50.00)
		Responders	1 (8.33)	2 (50.00)
		OR (95% CI)	0.09 (0.01, 1.55)	
		RR (95% CI)	0.17 (0.02, 1.38)	
		RD % (95% CI)	-41.67 (-93.10, 9.77)	
		p-value – Fisher's Exact Test	0.1357	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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FMS-500 responders ≥ 1 level by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (33.33)	0 (0.00)
		Non-Responders [2]	8 (88.89)	6 (85.71)
		Responders	1 (11.11)	1 (14.29)
		OR (95% CI)	0.75 (0.04, 14.58)	
		RR (95% CI)	0.78 (0.06, 10.37)	
		RD % (95% CI)	-3.17 (-36.24, 29.89)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	9 (100.00)	7 (100.00)

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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4.10.6.2.16 FMS-500 responders ≥ 1 level by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Region, p-value Chi-Square[1]	0.9977	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (12.50)	0 (0.00)
		Non-Responders [2]	7 (87.50)	5 (83.33)
		Responders	1 (12.50)	1 (16.67)
		OR (95% CI)	0.71 (0.04, 14.35)	
		RR (95% CI)	0.75 (0.06, 9.72)	
		RD % (95% CI)	-4.17 (-41.78, 33.44)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (12.50)	0 (0.00)
		Non-Responders [2]	7 (87.50)	4 (66.67)
		Responders	1 (12.50)	2 (33.33)
		OR (95% CI)	0.29 (0.02, 4.24)	
		RR (95% CI)	0.38 (0.04, 3.23)	
		RD % (95% CI)	-20.83 (-64.97, 23.30)	
		p-value – Fisher's Exact Test	0.5385	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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FMS-500 responders ≥ 1 level by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	4 (30.77)	0 (0.00)
		Non-Responders [2]	12 (92.31)	4 (80.00)
		Responders	1 (7.69)	1 (20.00)
		OR (95% CI)	0.33 (0.02, 6.65)	
		RR (95% CI)	0.38 (0.03, 5.04)	
		RD % (95% CI)	-12.31 (-50.24, 25.63)	
		p-value – Fisher's Exact Test	0.4902	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (15.38)	0 (0.00)
		Non-Responders [2]	13 (100.00)	5 (100.00)

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.6.2.17 FMS-500 responders ≥ 1 level by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.9753	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	8 (88.89)	4 (80.00)
		Responders	1 (11.11)	1 (20.00)
		OR (95% CI)	0.50 (0.02, 10.25)	
		RR (95% CI)	0.56 (0.04, 7.09)	
		RD % (95% CI)	-8.89 (-49.52, 31.74)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	8 (88.89)	4 (80.00)
		Responders	1 (11.11)	1 (20.00)
		OR (95% CI)	0.50 (0.02, 10.25)	
		RR (95% CI)	0.56 (0.04, 7.09)	
		RD % (95% CI)	-8.89 (-49.52, 31.74)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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FMS-500 responders ≥ 1 level by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	4 (33.33)	0 (0.00)
		Non-Responders [2]	11 (91.67)	5 (83.33)
		Responders	1 (8.33)	1 (16.67)
		OR (95% CI)	0.45 (0.02, 8.83)	
		RR (95% CI)	0.50 (0.04, 6.68)	
		RD % (95% CI)	-8.33 (-42.00, 25.34)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	12 (100.00)	5 (83.33)
		Responders	0 (0.00)	1 (16.67)
		OR (95% CI)	0.15 (0.01, 4.20)	
		RR (95% CI)	0.18 (0.01, 3.85)	
		RD % (95% CI)	-17.58 (-49.73, 14.56)	
		p-value – Fisher's Exact Test	0.3333	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.7 Subgruppenanalysen für den Endpunkt GFAQ

4.10.7.1 GFAQ by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.3178	
Male	Baseline	Absolute value	n (%)	12 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	8.08 (1.730)	7.00 (2.582)
	Week 12	Absolute value	n (%)	9 (75.00)	7 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			Mean (SD)	7.67 (2.646)	7.29 (2.812)
		Change from Baseline	n (%)	9 (75.00)	7 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-0.35 (0.352)	0.31 (0.406)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.66 (0.542)	
			95% CI for LS Mean Difference [2]	-1.83, 0.51	
			p-value MMRM [2]	0.2448	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.56	
			95% CI for SMD (Hedges' g)	-1.57, 0.45	
			p-value WRS[3]	0.4045	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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1.4.7 GFAQ
GFAQ by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	11 (91.67)	7 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	7.82 (2.040)	6.71 (2.752)
		Change from Baseline	n (%)	11 (91.67)	7 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-0.20 (0.285)	-0.26 (0.357)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.06 (0.463)	
			95% CI for LS Mean Difference [2]	-0.93, 1.04	
			p-value MMRM [2]	0.9049	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.05	
			95% CI for SMD (Hedges' g)	-0.89, 1.00	
			p-value WRS[3]	0.9166	
Female	Baseline	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	7.67 (2.500)	8.25 (2.872)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
Program: t-qs-cont-sub.sas
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1.4.7 GFAQ
GFAQ by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	8.38 (1.408)	8.00 (2.000)
		Change from Baseline	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-0.06 (0.220)	-0.23 (0.320)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.17 (0.389)	
			95% CI for LS Mean Difference [2]	-0.72, 1.06	
			p-value MMRM [2]	0.6694	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.24	
			95% CI for SMD (Hedges' g)	-0.97, 1.44	
			p-value WRS[3]	0.4566	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
Program: t-qs-cont-sub.sas
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1.4.7 GFAQ
GFAQ by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	8.11 (2.619)	8.00 (2.000)
		Change from Baseline	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.41 (0.223)	-0.23 (0.332)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.64 (0.401)	
			95% CI for LS Mean Difference [2]	-0.25, 1.53	
			p-value MMRM [2]	0.1414	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.84	
			95% CI for SMD (Hedges' g)	-0.39, 2.07	
			p-value WRS[3]	0.2098	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
Program: t-qs-cont-sub.sas
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4.10.7.2 GFAQ by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.5262	
<10.5 years old at screening	Baseline	Absolute value	n (%)	12 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	8.25 (1.765)	7.25 (2.500)
	Week 12	Absolute value	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	8.10 (1.969)	7.50 (2.380)
		Change from Baseline	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-0.09 (0.216)	0.20 (0.350)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.29 (0.415)	
			95% CI for LS Mean Difference [2]	-1.20, 0.61	
			p-value MMRM [2]	0.4925	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.39	
			95% CI for SMD (Hedges' g)	-1.56, 0.78	
			p-value WRS[3]	0.6693	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

NOTE: Median age used as cut-off point.

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GFAQ by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	8.36 (1.963)	7.50 (1.915)
		Change from Baseline	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.20 (0.213)	0.20 (0.356)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.00 (0.419)	
			95% CI for LS Mean Difference [2]	-0.91, 0.91	
			p-value MMRM [2]	0.9983	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.00	
			95% CI for SMD (Hedges' g)	-1.15, 1.14	
			p-value WRS[3]	0.7949	
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	7.44 (2.404)	7.57 (2.878)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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GFAQ by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	7 (77.78)	7 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	7.86 (2.478)	7.57 (2.699)
		Change from Baseline	n (%)	7 (77.78)	7 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-0.36 (0.441)	-0.00 (0.453)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.36 (0.633)	
			95% CI for LS Mean Difference [2]	-1.76, 1.04	
			p-value MMRM [2]	0.5804	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.27	
			95% CI for SMD (Hedges' g)	-1.32, 0.78	
			p-value WRS[3]	1.0000	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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GFAQ by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	7.44 (2.603)	7.00 (2.887)
		Change from Baseline	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-0.00 (0.316)	-0.57 (0.358)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.57 (0.477)	
			95% CI for LS Mean Difference [2]	-0.46, 1.60	
			p-value MMRM [2]	0.2539	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.55	
			95% CI for SMD (Hedges' g)	-0.46, 1.55	
			p-value WRS[3]	0.2361	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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4.10.7.3 GFAQ by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.7314	
US	Baseline	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	8.25 (1.669)	7.50 (2.881)
	Week 12	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	8.13 (2.475)	7.67 (3.141)
		Change from Baseline	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-0.11 (0.394)	0.15 (0.456)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.27 (0.605)	
			95% CI for LS Mean Difference [2]	-1.60, 1.07	
			p-value MMRM [2]	0.6666	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.21	
			95% CI for SMD (Hedges' g)	-1.27, 0.85	
			p-value WRS[3]	0.8135	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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GFAQ by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	8.50 (1.927)	7.50 (2.811)
		Change from Baseline	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.26 (0.252)	-0.01 (0.292)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.27 (0.390)	
			95% CI for LS Mean Difference [2]	-0.58, 1.13	
			p-value MMRM [2]	0.4967	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.34	
			95% CI for SMD (Hedges' g)	-0.73, 1.41	
			p-value WRS[3]	0.6350	
Non-US	Baseline	Absolute value	n (%)	13 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	7.69 (2.287)	7.40 (2.608)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
Program: t-qs-cont-sub.sas
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GFAQ by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	9 (69.23)	5 (100.00)
			Number of patients with missing data: n (%)	4 (30.77)	0 (0.00)
			Mean (SD)	7.89 (1.900)	7.40 (1.673)
		Change from Baseline	n (%)	9 (69.23)	5 (100.00)
			Number of patients with missing data: n (%)	4 (30.77)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-0.14 (0.230)	-0.03 (0.307)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.11 (0.385)	
			95% CI for LS Mean Difference [2]	-0.95, 0.74	
			p-value MMRM [2]	0.7842	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.14	
			95% CI for SMD (Hedges' g)	-1.23, 0.95	
			p-value WRS[3]	1.0000	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
Program: t-qs-cont-sub.sas
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GFAQ by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	12 (92.31)	5 (100.00)
			Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
			Mean (SD)	7.58 (2.466)	6.80 (2.280)
		Change from Baseline	n (%)	12 (92.31)	5 (100.00)
			Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-0.01 (0.274)	-0.63 (0.425)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.63 (0.506)	
			95% CI for LS Mean Difference [2]	-0.46, 1.71	
			p-value MMRM [2]	0.2365	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.60	
			95% CI for SMD (Hedges' g)	-0.46, 1.67	
			p-value WRS[3]	0.2654	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.7.4 GFAQ by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.0912	
I	Baseline	Absolute value	n (%)	9 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	9.11 (0.782)	9.60 (0.548)
	Week 12	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	9.38 (0.744)	9.40 (0.548)
		Change from Baseline	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.14 (0.219)	-0.03 (0.279)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.17 (0.357)	
			95% CI for LS Mean Difference [2]	-0.61, 0.95	
			p-value MMRM [2]	0.6392	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.25	
			95% CI for SMD (Hedges' g)	-0.88, 1.37	
			p-value WRS[3]	0.4545	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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GFAQ by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	9.50 (0.535)	9.00 (0.000)
		Change from Baseline	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.27 (0.112)	-0.43 (0.143)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.70 (0.187)	
			95% CI for LS Mean Difference [2]	0.28, 1.11	
			p-value MMRM [2]	0.0036 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.94	
			95% CI for SMD (Hedges' g)	0.56, 3.32	
			p-value WRS[3]	0.0326 ***	
≥ II	Baseline	Absolute value	n (%)	12 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	7.00 (2.256)	5.67 (2.251)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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GFAQ by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	9 (75.00)	6 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			Mean (SD)	6.78 (2.224)	6.00 (2.366)
		Change from Baseline	n (%)	9 (75.00)	6 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-0.53 (0.328)	0.33 (0.408)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.86 (0.534)	
			95% CI for LS Mean Difference [2]	-2.01, 0.29	
			p-value MMRM [2]	0.1295	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.79	
			95% CI for SMD (Hedges' g)	-1.87, 0.28	
			p-value WRS[3]	0.0983	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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GFAQ by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	12 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	6.92 (2.392)	5.67 (2.503)
		Change from Baseline	n (%)	12 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-0.08 (0.289)	-0.00 (0.415)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.08 (0.515)	
			95% CI for LS Mean Difference [2]	-1.18, 1.01	
			p-value MMRM [2]	0.8737	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.08	
			95% CI for SMD (Hedges' g)	-1.06, 0.90	
			p-value WRS[3]	0.8236	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.7.5 GFAQ responders ≥ 2 level by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Gender, p-value Chi-Square[1]	Not done	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (25.00)	0 (0.00)
		Non-Responders [2]	12 (100.00)	7 (100.00)
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [2]	12 (100.00)	7 (100.00)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	9 (100.00)	4 (100.00)
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	9 (100.00)	4 (100.00)

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.7.6 GFAQ responders ≥ 2 level by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Age Group, p-value Chi-Square[1]	Not done	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	12 (100.00)	4 (100.00)
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [2]	12 (100.00)	4 (100.00)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (22.22)	0 (0.00)
		Non-Responders [2]	9 (100.00)	7 (100.00)
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	9 (100.00)	7 (100.00)

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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4.10.7.7 GFAQ responders ≥ 2 level by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Region, p-value Chi-Square[1]	Not done	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	8 (100.00)	6 (100.00)
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	8 (100.00)	6 (100.00)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	4 (30.77)	0 (0.00)
		Non-Responders [2]	13 (100.00)	5 (100.00)
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (7.69)	0 (0.00)
		Non-Responders [2]	13 (100.00)	5 (100.00)

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.7.8 GFAQ responders ≥ 2 level by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	Not done	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	9 (100.00)	5 (100.00)
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	9 (100.00)	5 (100.00)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (25.00)	0 (0.00)
		Non-Responders [2]	12 (100.00)	6 (100.00)
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	12 (100.00)	6 (100.00)

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.8 Subgruppenanalysen für den Endpunkt VABS-II

4.10.8.1 VABS-II Adaptive Behavior Composite Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.2030	
Male	Baseline	Absolute value	n (%)	11 (91.67)	7 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	69.73 (24.405)	70.43 (17.850)
	Week 12	Absolute value	n (%)	10 (83.33)	6 (85.71)
			Number of patients with missing data: n (%)	2 (16.67)	1 (14.29)
			Mean (SD)	76.60 (21.506)	74.17 (18.904)
		Change from Baseline	n (%)	10 (83.33)	6 (85.71)
			Number of patients with missing data: n (%)	2 (16.67)	1 (14.29)
			LS Mean Change from Baseline (SE) [2]	5.93 (5.461)	2.28 (7.052)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.65 (8.924)	
			95% CI for LS Mean Difference [2]	-15.53, 22.82	
			p-value MMRM [2]	0.6891	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.19	
			95% CI for SMD (Hedges' g)	-0.82, 1.21	
			p-value WRS[3]	0.5089	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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1.4.8 VABS-II
VABS-II Adaptive Behavior Composite Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	10 (83.33)	6 (85.71)
			Number of patients with missing data: n (%)	2 (16.67)	1 (14.29)
			Mean (SD)	75.30 (19.189)	67.83 (12.937)
		Change from Baseline	n (%)	10 (83.33)	6 (85.71)
			Number of patients with missing data: n (%)	2 (16.67)	1 (14.29)
			LS Mean Change from Baseline (SE) [2]	4.63 (4.168)	-4.05 (5.382)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	8.68 (6.812)	
			95% CI for LS Mean Difference [2]	-6.01, 23.37	
			p-value MMRM [2]	0.2246	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.60	
			95% CI for SMD (Hedges' g)	-0.44, 1.63	
			p-value WRS[3]	0.3113	
Female	Baseline	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	73.78 (25.543)	61.75 (7.676)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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1.4.8 VABS-II
VABS-II Adaptive Behavior Composite Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	8 (88.89)	3 (75.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (25.00)
			Mean (SD)	75.88 (24.649)	71.00 (10.536)
		Change from Baseline	n (%)	8 (88.89)	3 (75.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	1.27 (3.091)	4.70 (4.946)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-3.42 (5.802)	
			95% CI for LS Mean Difference [2]	-16.34, 9.49	
			p-value MMRM [2]	0.5682	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.34	
			95% CI for SMD (Hedges' g)	-1.68, 0.99	
			p-value WRS[3]	0.2606	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
Program: t-qs-cont-sub.sas
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1.4.8 VABS-II
VABS-II Adaptive Behavior Composite Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	77.38 (11.057)	65.00 (6.272)
		Change from Baseline	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-2.75 (2.316)	0.41 (3.692)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-3.16 (4.451)	
			95% CI for LS Mean Difference [2]	-13.09, 6.77	
			p-value MMRM [2]	0.4944	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.41	
			95% CI for SMD (Hedges' g)	-1.62, 0.81	
			p-value WRS[3]	0.2141	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
Program: t-qs-cont-sub.sas
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4.10.8.2 VABS-II Adaptive Behavior Composite Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.9775	
<10.5 years old at screening	Baseline	Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	75.18 (26.011)	66.25 (10.595)
	Week 12	Absolute value	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	81.30 (18.839)	66.50 (12.342)
		Change from Baseline	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	6.67 (4.920)	-3.68 (7.793)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	10.36 (9.233)	
			95% CI for LS Mean Difference [2]	-9.76, 30.47	
			p-value MMRM [2]	0.2839	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.60	
			95% CI for SMD (Hedges' g)	-0.59, 1.78	
			p-value WRS[3]	0.6124	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

NOTE: Median age used as cut-off point.

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VABS-II Adaptive Behavior Composite Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	77.40 (14.645)	64.25 (11.471)
		Change from Baseline	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	2.77 (3.324)	-5.93 (5.277)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	8.71 (6.260)	
			95% CI for LS Mean Difference [2]	-4.95, 22.36	
			p-value MMRM [2]	0.1898	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.74	
			95% CI for SMD (Hedges' g)	-0.45, 1.94	
			p-value WRS[3]	0.9740	
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	67.11 (22.828)	67.86 (17.967)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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VABS-II Adaptive Behavior Composite Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	8 (88.89)	5 (71.43)
			Number of patients with missing data: n (%)	1 (11.11)	2 (28.57)
			Mean (SD)	70.00 (25.790)	78.40 (17.729)
		Change from Baseline	n (%)	8 (88.89)	5 (71.43)
			Number of patients with missing data: n (%)	1 (11.11)	2 (28.57)
			LS Mean Change from Baseline (SE) [2]	1.34 (3.196)	6.70 (3.939)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-5.35 (5.070)	
			95% CI for LS Mean Difference [2]	-16.41, 5.71	
			p-value MMRM [2]	0.3123	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.54	
			95% CI for SMD (Hedges' g)	-1.68, 0.60	
			p-value WRS[3]	0.3699	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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VABS-II Adaptive Behavior Composite Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	8 (88.89)	6 (85.71)
			Number of patients with missing data: n (%)	1 (11.11)	1 (14.29)
			Mean (SD)	74.75 (17.839)	68.33 (10.386)
		Change from Baseline	n (%)	8 (88.89)	6 (85.71)
			Number of patients with missing data: n (%)	1 (11.11)	1 (14.29)
			LS Mean Change from Baseline (SE) [2]	1.25 (3.696)	-1.45 (4.390)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.70 (5.725)	
			95% CI for LS Mean Difference [2]	-9.85, 15.25	
			p-value MMRM [2]	0.6458	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.23	
			95% CI for SMD (Hedges' g)	-0.83, 1.29	
			p-value WRS[3]	0.7346	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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4.10.8.3 VABS-II Adaptive Behavior Composite Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.7888	
US	Baseline	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	82.38 (11.326)	68.33 (13.382)
	Week 12	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	81.38 (10.070)	68.67 (11.483)
		Change from Baseline	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.70 (2.084)	-1.93 (2.447)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.63 (3.393)	
			95% CI for LS Mean Difference [2]	-4.70, 9.97	
			p-value MMRM [2]	0.4518	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.40	
			95% CI for SMD (Hedges' g)	-0.67, 1.47	
			p-value WRS[3]	0.8751	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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VABS-II Adaptive Behavior Composite Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	78.88 (8.184)	65.67 (11.501)
		Change from Baseline	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-1.80 (1.670)	-4.93 (1.979)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.13 (2.808)	
			95% CI for LS Mean Difference [2]	-3.05, 9.31	
			p-value MMRM [2]	0.2885	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.58	
			95% CI for SMD (Hedges' g)	-0.50, 1.67	
			p-value WRS[3]	0.8775	
Non-US	Baseline	Absolute value	n (%)	12 (92.31)	5 (100.00)
			Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
			Mean (SD)	64.33 (28.279)	66.00 (18.507)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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VABS-II Adaptive Behavior Composite Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	10 (76.92)	3 (60.00)
			Number of patients with missing data: n (%)	3 (23.08)	2 (40.00)
			Mean (SD)	72.20 (28.545)	82.00 (22.517)
		Change from Baseline	n (%)	10 (76.92)	3 (60.00)
			Number of patients with missing data: n (%)	3 (23.08)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	5.43 (6.031)	11.03 (10.156)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-5.60 (11.806)	
			95% CI for LS Mean Difference [2]	-31.07, 19.87	
			p-value MMRM [2]	0.6431	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.27	
			95% CI for SMD (Hedges' g)	-1.56, 1.03	
			p-value WRS[3]	0.1748	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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VABS-II Adaptive Behavior Composite Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	10 (76.92)	4 (80.00)
			Number of patients with missing data: n (%)	3 (23.08)	1 (20.00)
			Mean (SD)	74.10 (20.052)	68.25 (9.946)
		Change from Baseline	n (%)	10 (76.92)	4 (80.00)
			Number of patients with missing data: n (%)	3 (23.08)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	3.78 (4.633)	0.13 (7.587)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.65 (8.892)	
			95% CI for LS Mean Difference [2]	-15.83, 23.12	
			p-value MMRM [2]	0.6892	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.22	
			95% CI for SMD (Hedges' g)	-0.94, 1.38	
			p-value WRS[3]	1.0000	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.8.4 VABS-II Adaptive Behavior Composite Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.6154	
I	Baseline	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	84.38 (12.727)	70.40 (12.857)
	Week 12	Absolute value	n (%)	8 (88.89)	4 (80.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (20.00)
			Mean (SD)	84.38 (12.872)	79.00 (5.477)
		Change from Baseline	n (%)	8 (88.89)	4 (80.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	1.88 (3.325)	1.79 (4.560)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.08 (6.010)	
			95% CI for LS Mean Difference [2]	-13.31, 13.47	
			p-value MMRM [2]	0.9890	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.01	
			95% CI for SMD (Hedges' g)	-1.19, 1.21	
			p-value WRS[3]	0.6828	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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VABS-II Adaptive Behavior Composite Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	82.50 (14.010)	71.60 (8.295)
		Change from Baseline	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.00 (3.584)	-2.81 (4.869)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.82 (6.411)	
			95% CI for LS Mean Difference [2]	-11.35, 16.99	
			p-value MMRM [2]	0.6691	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.24	
			95% CI for SMD (Hedges' g)	-0.88, 1.36	
			p-value WRS[3]	0.5113	
≥ II	Baseline	Absolute value	n (%)	12 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	63.00 (26.850)	64.67 (17.489)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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VABS-II Adaptive Behavior Composite Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	10 (83.33)	5 (83.33)
			Number of patients with missing data: n (%)	2 (16.67)	1 (16.67)
			Mean (SD)	69.80 (26.486)	68.40 (20.550)
		Change from Baseline	n (%)	10 (83.33)	5 (83.33)
			Number of patients with missing data: n (%)	2 (16.67)	1 (16.67)
			LS Mean Change from Baseline (SE) [2]	4.61 (5.728)	2.42 (8.409)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.19 (10.176)	
			95% CI for LS Mean Difference [2]	-19.74, 24.12	
			p-value MMRM [2]	0.8326	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.11	
			95% CI for SMD (Hedges' g)	-0.97, 1.18	
			p-value WRS[3]	0.3556	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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VABS-II Adaptive Behavior Composite Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	10 (83.33)	5 (83.33)
			Number of patients with missing data: n (%)	2 (16.67)	1 (16.67)
			Mean (SD)	71.20 (15.803)	61.80 (10.710)
		Change from Baseline	n (%)	10 (83.33)	5 (83.33)
			Number of patients with missing data: n (%)	2 (16.67)	1 (16.67)
			LS Mean Change from Baseline (SE) [2]	3.00 (3.529)	-4.18 (5.194)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	7.18 (6.280)	
			95% CI for LS Mean Difference [2]	-6.44, 20.81	
			p-value MMRM [2]	0.2741	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.57	
			95% CI for SMD (Hedges' g)	-0.52, 1.67	
			p-value WRS[3]	0.4948	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.8.5 VABS-II Adaptive Behavior Composite Score responders ≥ 7,5 by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Gender, p-value Chi-Square[1]	0.9760	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (14.29)
		Non-Responders [2]	10 (83.33)	7 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	3.57 (0.15, 85.68)	
		RR (95% CI)	3.08 (0.17, 56.25)	
		RD % (95% CI)	12.98 (-14.23, 40.19)	
		p-value – Fisher's Exact Test	0.5088	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (14.29)
		Non-Responders [2]	10 (83.33)	7 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	3.57 (0.15, 85.68)	
		RR (95% CI)	3.08 (0.17, 56.25)	
		RD % (95% CI)	12.98 (-14.23, 40.19)	
		p-value – Fisher's Exact Test	0.5088	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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VABS-II Adaptive Behavior Composite Score responders ≥ 7,5 by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (25.00)
		Non-Responders [2]	8 (88.89)	3 (75.00)
		Responders	1 (11.11)	1 (25.00)
		OR (95% CI)	0.38 (0.02, 8.10)	
		RR (95% CI)	0.44 (0.04, 5.46)	
		RD % (95% CI)	-13.89 (-61.03, 33.25)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	8 (88.89)	3 (75.00)
		Responders	1 (11.11)	1 (25.00)
		OR (95% CI)	0.38 (0.02, 8.10)	
		RR (95% CI)	0.44 (0.04, 5.46)	
		RD % (95% CI)	-13.89 (-61.03, 33.25)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.8.6 VABS-II Adaptive Behavior Composite Score responders ≥ 7,5 by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Age Group, p-value Chi-Square[1]	0.9774	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	10 (83.33)	4 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	2.14 (0.08, 54.22)	
		RR (95% CI)	1.92 (0.11, 33.44)	
		RD % (95% CI)	9.23 (-24.69, 43.15)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	11 (91.67)	4 (100.00)
		Responders	1 (8.33)	0 (0.00)
		OR (95% CI)	1.17 (0.04, 34.52)	
		RR (95% CI)	1.15 (0.06, 23.88)	
		RD % (95% CI)	1.54 (-29.97, 33.05)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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VABS-II Adaptive Behavior Composite Score responders ≥ 7,5 by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	2 (28.57)
		Non-Responders [2]	8 (88.89)	6 (85.71)
		Responders	1 (11.11)	1 (14.29)
		OR (95% CI)	0.75 (0.04, 14.58)	
		RR (95% CI)	0.78 (0.06, 10.37)	
		RD % (95% CI)	-3.17 (-36.24, 29.89)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (14.29)
		Non-Responders [2]	7 (77.78)	6 (85.71)
		Responders	2 (22.22)	1 (14.29)
		OR (95% CI)	1.71 (0.12, 23.94)	
		RR (95% CI)	1.56 (0.17, 13.87)	
		RD % (95% CI)	7.94 (-29.61, 45.48)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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4.10.8.7 VABS-II Adaptive Behavior Composite Score responders ≥ 7,5 by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Region, p-value Chi-Square[1]	0.9996	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	7 (87.50)	6 (100.00)
		Responders	1 (12.50)	0 (0.00)
		OR (95% CI)	2.60 (0.09, 75.49)	
		RR (95% CI)	2.33 (0.11, 48.99)	
		RD % (95% CI)	9.52 (-21.41, 40.46)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	8 (100.00)	6 (100.00)

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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VABS-II Adaptive Behavior Composite Score responders ≥ 7,5 by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (23.08)	2 (40.00)
		Non-Responders [2]	11 (84.62)	4 (80.00)
		Responders	2 (15.38)	1 (20.00)
		OR (95% CI)	0.73 (0.05, 10.39)	
		RR (95% CI)	0.77 (0.09, 6.72)	
		RD % (95% CI)	-4.62 (-44.79, 35.56)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (23.08)	1 (20.00)
		Non-Responders [2]	10 (76.92)	4 (80.00)
		Responders	3 (23.08)	1 (20.00)
		OR (95% CI)	1.20 (0.09, 15.26)	
		RR (95% CI)	1.15 (0.15, 8.65)	
		RD % (95% CI)	3.08 (-38.80, 44.96)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.8.8 VABS-II Adaptive Behavior Composite Score responders ≥ 7,5 by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.9668	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (20.00)
		Non-Responders [2]	8 (88.89)	4 (80.00)
		Responders	1 (11.11)	1 (20.00)
		OR (95% CI)	0.50 (0.02, 10.25)	
		RR (95% CI)	0.56 (0.04, 7.09)	
		RD % (95% CI)	-8.89 (-49.52, 31.74)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	8 (88.89)	4 (80.00)
		Responders	1 (11.11)	1 (20.00)
		OR (95% CI)	0.50 (0.02, 10.25)	
		RR (95% CI)	0.56 (0.04, 7.09)	
		RD % (95% CI)	-8.89 (-49.52, 31.74)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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VABS-II Adaptive Behavior Composite Score responders ≥ 7,5 by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (16.67)
		Non-Responders [2]	10 (83.33)	6 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	3.10 (0.13, 75.18)	
		RR (95% CI)	2.69 (0.15, 48.64)	
		RD % (95% CI)	12.09 (-16.60, 40.78)	
		p-value – Fisher's Exact Test	0.5294	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (16.67)
		Non-Responders [2]	10 (83.33)	6 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	3.10 (0.13, 75.18)	
		RR (95% CI)	2.69 (0.15, 48.64)	
		RD % (95% CI)	12.09 (-16.60, 40.78)	
		p-value – Fisher's Exact Test	0.5294	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.8.9 VABS-II Communication Domain Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.8852	
Male	Baseline	Absolute value	n (%)	11 (91.67)	7 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	71.18 (17.854)	81.57 (28.041)
	Week 12	Absolute value	n (%)	10 (83.33)	6 (85.71)
			Number of patients with missing data: n (%)	2 (16.67)	1 (14.29)
			Mean (SD)	71.20 (23.237)	80.00 (22.163)
		Change from Baseline	n (%)	10 (83.33)	6 (85.71)
			Number of patients with missing data: n (%)	2 (16.67)	1 (14.29)
			LS Mean Change from Baseline (SE) [2]	-1.55 (2.955)	-3.75 (3.779)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.20 (4.851)	
			95% CI for LS Mean Difference [2]	-8.10, 12.49	
			p-value MMRM [2]	0.6570	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.22	
			95% CI for SMD (Hedges' g)	-0.80, 1.23	
			p-value WRS[3]	0.3252	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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VABS-II Communication Domain Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	11 (91.67)	7 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	68.82 (20.173)	76.43 (19.277)
		Change from Baseline	n (%)	11 (91.67)	7 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-3.14 (2.435)	-4.31 (3.038)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.17 (3.953)	
			95% CI for LS Mean Difference [2]	-7.26, 9.59	
			p-value MMRM [2]	0.7720	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.13	
			95% CI for SMD (Hedges' g)	-0.82, 1.08	
			p-value WRS[3]	0.4634	
Female	Baseline	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	71.78 (25.999)	58.25 (26.513)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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VABS-II Communication Domain Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	8 (88.89)	3 (75.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (25.00)
			Mean (SD)	78.25 (28.524)	55.67 (30.892)
		Change from Baseline	n (%)	8 (88.89)	3 (75.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	2.32 (2.329)	-0.95 (3.875)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.28 (4.575)	
			95% CI for LS Mean Difference [2]	-7.14, 13.70	
			p-value MMRM [2]	0.4928	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.42	
			95% CI for SMD (Hedges' g)	-0.92, 1.76	
			p-value WRS[3]	0.3515	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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VABS-II Communication Domain Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	69.44 (26.562)	54.25 (22.867)
		Change from Baseline	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-2.33 (1.713)	-4.01 (2.635)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.68 (3.175)	
			95% CI for LS Mean Difference [2]	-5.39, 8.76	
			p-value MMRM [2]	0.6074	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.29	
			95% CI for SMD (Hedges' g)	-0.90, 1.47	
			p-value WRS[3]	0.7888	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.8.10 VABS-II Communication Domain Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.4060	
<10.5 years old at screening	Baseline	Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	76.64 (19.526)	57.50 (26.413)
	Week 12	Absolute value	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	78.20 (25.337)	57.50 (26.413)
		Change from Baseline	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.45 (2.857)	-0.48 (4.726)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.94 (5.601)	
			95% CI for LS Mean Difference [2]	-11.19, 13.06	
			p-value MMRM [2]	0.8700	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.09	
			95% CI for SMD (Hedges' g)	-1.07, 1.25	
			p-value WRS[3]	0.5934	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

NOTE: Median age used as cut-off point.

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VABS-II Communication Domain Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	74.00 (20.025)	57.25 (26.323)
		Change from Baseline	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-2.48 (1.821)	-0.73 (3.181)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.74 (3.791)	
			95% CI for LS Mean Difference [2]	-10.00, 6.52	
			p-value MMRM [2]	0.6540	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.26	
			95% CI for SMD (Hedges' g)	-1.40, 0.89	
			p-value WRS[3]	0.8593	
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	65.11 (22.713)	82.00 (27.659)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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VABS-II Communication Domain Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	8 (88.89)	5 (71.43)
			Number of patients with missing data: n (%)	1 (11.11)	2 (28.57)
			Mean (SD)	69.50 (25.807)	83.40 (22.165)
		Change from Baseline	n (%)	8 (88.89)	5 (71.43)
			Number of patients with missing data: n (%)	1 (11.11)	2 (28.57)
			LS Mean Change from Baseline (SE) [2]	0.24 (2.743)	-4.91 (3.555)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	5.15 (4.629)	
			95% CI for LS Mean Difference [2]	-4.92, 15.23	
			p-value MMRM [2]	0.2871	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.59	
			95% CI for SMD (Hedges' g)	-0.56, 1.73	
			p-value WRS[3]	0.0490 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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VABS-II Communication Domain Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	63.11 (25.295)	74.71 (19.129)
		Change from Baseline	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-2.93 (2.646)	-6.55 (2.940)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.62 (4.061)	
			95% CI for LS Mean Difference [2]	-5.11, 12.35	
			p-value MMRM [2]	0.3876	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.42	
			95% CI for SMD (Hedges' g)	-0.58, 1.42	
			p-value WRS[3]	0.3926	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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4.10.8.11 VABS-II Communication Domain Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.6960	
US	Baseline	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	80.63 (11.612)	75.67 (15.578)
	Week 12	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	79.00 (9.871)	72.33 (10.386)
		Change from Baseline	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-1.03 (1.887)	-4.13 (2.185)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.10 (2.913)	
			95% CI for LS Mean Difference [2]	-3.32, 9.51	
			p-value MMRM [2]	0.3108	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.52	
			95% CI for SMD (Hedges' g)	-0.56, 1.59	
			p-value WRS[3]	0.6300	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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VABS-II Communication Domain Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	78.50 (9.502)	72.50 (13.605)
		Change from Baseline	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-1.53 (1.800)	-3.96 (2.084)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.43 (2.781)	
			95% CI for LS Mean Difference [2]	-3.70, 8.55	
			p-value MMRM [2]	0.4011	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.42	
			95% CI for SMD (Hedges' g)	-0.65, 1.50	
			p-value WRS[3]	0.2657	
Non-US	Baseline	Absolute value	n (%)	12 (92.31)	5 (100.00)
			Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
			Mean (SD)	65.33 (24.366)	70.00 (41.563)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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VABS-II Communication Domain Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	10 (76.92)	3 (60.00)
			Number of patients with missing data: n (%)	3 (23.08)	2 (40.00)
			Mean (SD)	70.60 (32.965)	71.00 (50.030)
		Change from Baseline	n (%)	10 (76.92)	3 (60.00)
			Number of patients with missing data: n (%)	3 (23.08)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	1.97 (3.354)	-1.31 (5.991)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.28 (6.878)	
			95% CI for LS Mean Difference [2]	-11.93, 18.49	
			p-value MMRM [2]	0.6433	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.27	
			95% CI for SMD (Hedges' g)	-1.02, 1.57	
			p-value WRS[3]	0.1503	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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VABS-II Communication Domain Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	12 (92.31)	5 (100.00)
			Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
			Mean (SD)	62.83 (26.809)	63.40 (31.222)
		Change from Baseline	n (%)	12 (92.31)	5 (100.00)
			Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-2.72 (2.338)	-6.47 (3.607)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.75 (4.305)	
			95% CI for LS Mean Difference [2]	-5.50, 13.00	
			p-value MMRM [2]	0.3985	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.42	
			95% CI for SMD (Hedges' g)	-0.63, 1.48	
			p-value WRS[3]	0.9837	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.8.12 VABS-II Communication Domain Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.8034	
I	Baseline	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	82.63 (11.109)	79.80 (15.659)
	Week 12	Absolute value	n (%)	8 (88.89)	4 (80.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (20.00)
			Mean (SD)	82.75 (13.646)	79.00 (6.683)
		Change from Baseline	n (%)	8 (88.89)	4 (80.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	0.19 (3.074)	-4.47 (4.271)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	4.66 (5.263)	
			95% CI for LS Mean Difference [2]	-7.01, 16.33	
			p-value MMRM [2]	0.3958	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.47	
			95% CI for SMD (Hedges' g)	-0.74, 1.69	
			p-value WRS[3]	0.2949	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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VABS-II Communication Domain Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	80.63 (11.575)	75.00 (13.748)
		Change from Baseline	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-1.94 (2.613)	-5.42 (3.335)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.48 (4.242)	
			95% CI for LS Mean Difference [2]	-5.95, 12.92	
			p-value MMRM [2]	0.4302	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.41	
			95% CI for SMD (Hedges' g)	-0.72, 1.54	
			p-value WRS[3]	0.5493	
≥ II	Baseline	Absolute value	n (%)	12 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	64.00 (23.487)	67.50 (36.926)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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VABS-II Communication Domain Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	10 (83.33)	5 (83.33)
			Number of patients with missing data: n (%)	2 (16.67)	1 (16.67)
			Mean (SD)	67.60 (30.646)	66.20 (35.534)
		Change from Baseline	n (%)	10 (83.33)	5 (83.33)
			Number of patients with missing data: n (%)	2 (16.67)	1 (16.67)
			LS Mean Change from Baseline (SE) [2]	0.59 (2.666)	-2.17 (3.769)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.76 (4.620)	
			95% CI for LS Mean Difference [2]	-7.33, 12.86	
			p-value MMRM [2]	0.5614	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.29	
			95% CI for SMD (Hedges' g)	-0.79, 1.37	
			p-value WRS[3]	0.3223	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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VABS-II Communication Domain Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	12 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	61.42 (25.239)	62.83 (27.896)
		Change from Baseline	n (%)	12 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-2.78 (1.947)	-4.56 (2.746)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.78 (3.370)	
			95% CI for LS Mean Difference [2]	-5.41, 8.98	
			p-value MMRM [2]	0.6046	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.24	
			95% CI for SMD (Hedges' g)	-0.74, 1.23	
			p-value WRS[3]	0.8383	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.8.13 VABS-II Communication Domain Score responders ≥ 7,5 by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Gender, p-value Chi-Square[1]	0.9779	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (14.29)
		Non-Responders [2]	11 (91.67)	7 (100.00)
		Responders	1 (8.33)	0 (0.00)
		OR (95% CI)	1.96 (0.07, 54.67)	
		RR (95% CI)	1.85 (0.09, 40.05)	
		RD % (95% CI)	5.29 (-18.86, 29.43)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [2]	11 (91.67)	7 (100.00)
		Responders	1 (8.33)	0 (0.00)
		OR (95% CI)	1.96 (0.07, 54.67)	
		RR (95% CI)	1.85 (0.09, 40.05)	
		RD % (95% CI)	5.29 (-18.86, 29.43)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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VABS-II Communication Domain Score responders ≥ 7,5 by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (25.00)
		Non-Responders [2]	8 (88.89)	4 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	1.59 (0.05, 47.52)	
		RR (95% CI)	1.50 (0.07, 30.59)	
		RD % (95% CI)	5.00 (-29.37, 39.37)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	9 (100.00)	4 (100.00)

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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4.10.8.14 VABS-II Communication Domain Score responders ≥ 7,5 by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Age Group, p-value Chi-Square[1]	0.9766	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	11 (91.67)	4 (100.00)
		Responders	1 (8.33)	0 (0.00)
		OR (95% CI)	1.17 (0.04, 34.52)	
		RR (95% CI)	1.15 (0.06, 23.88)	
		RD % (95% CI)	1.54 (-29.97, 33.05)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [2]	12 (100.00)	4 (100.00)

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
Program: t-qs-categ-sub.sas
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VABS-II Communication Domain Score responders ≥ 7,5 by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	2 (28.57)
		Non-Responders [2]	8 (88.89)	7 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	2.65 (0.09, 75.29)	
		RR (95% CI)	2.40 (0.11, 51.32)	
		RD % (95% CI)	8.75 (-19.02, 36.52)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	8 (88.89)	7 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	2.65 (0.09, 75.29)	
		RR (95% CI)	2.40 (0.11, 51.32)	
		RD % (95% CI)	8.75 (-19.02, 36.52)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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4.10.8.15 VABS-II Communication Domain Score responders ≥ 7,5 by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Region, p-value Chi-Square[1]	0.9779	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	8 (100.00)	6 (100.00)
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	8 (100.00)	6 (100.00)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (23.08)	2 (40.00)
		Non-Responders [2]	11 (84.62)	5 (100.00)
		Responders	2 (15.38)	0 (0.00)
		OR (95% CI)	2.39 (0.10, 58.77)	
		RR (95% CI)	2.14 (0.12, 38.24)	
		RD % (95% CI)	9.52 (-20.34, 39.38)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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VABS-II Communication Domain Score responders ≥ 7,5 by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (7.69)	0 (0.00)
		Non-Responders [2]	12 (92.31)	5 (100.00)
		Responders	1 (7.69)	0 (0.00)
		OR (95% CI)	1.32 (0.05, 37.78)	
		RR (95% CI)	1.29 (0.06, 27.27)	
		RD % (95% CI)	2.38 (-25.03, 29.80)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.8.16 VABS-II Communication Domain Score responders ≥ 7,5 by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.9759	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (20.00)
		Non-Responders [2]	8 (88.89)	5 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	1.94 (0.07, 56.76)	
		RR (95% CI)	1.80 (0.09, 37.49)	
		RD % (95% CI)	6.67 (-24.62, 37.95)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	8 (88.89)	5 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	1.94 (0.07, 56.76)	
		RR (95% CI)	1.80 (0.09, 37.49)	
		RD % (95% CI)	6.67 (-24.62, 37.95)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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VABS-II Communication Domain Score responders ≥ 7,5 by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (16.67)
		Non-Responders [2]	11 (91.67)	6 (100.00)
		Responders	1 (8.33)	0 (0.00)
		OR (95% CI)	1.70 (0.06, 47.95)	
		RR (95% CI)	1.62 (0.08, 34.66)	
		RD % (95% CI)	4.40 (-21.40, 30.19)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	12 (100.00)	6 (100.00)

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.8.17 VABS-II Daily Living Skills Domain Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.0154 ***	
Male	Baseline	Absolute value	n (%)	11 (91.67)	7 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	69.27 (19.463)	65.71 (19.405)
	Week 12	Absolute value	n (%)	10 (83.33)	6 (85.71)
			Number of patients with missing data: n (%)	2 (16.67)	1 (14.29)
			Mean (SD)	73.40 (24.052)	72.67 (17.212)
		Change from Baseline	n (%)	10 (83.33)	6 (85.71)
			Number of patients with missing data: n (%)	2 (16.67)	1 (14.29)
			LS Mean Change from Baseline (SE) [2]	3.62 (2.548)	4.79 (3.255)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.16 (4.138)	
			95% CI for LS Mean Difference [2]	-9.95, 7.62	
			p-value MMRM [2]	0.7820	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.13	
			95% CI for SMD (Hedges' g)	-1.15, 0.88	
			p-value WRS[3]	0.4108	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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VABS-II Daily Living Skills Domain Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	11 (91.67)	7 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	70.73 (22.222)	60.57 (17.155)
		Change from Baseline	n (%)	11 (91.67)	7 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	1.46 (2.101)	-5.16 (2.646)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	6.62 (3.384)	
			95% CI for LS Mean Difference [2]	-0.59, 13.83	
			p-value MMRM [2]	0.0692	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.87	
			95% CI for SMD (Hedges' g)	-0.12, 1.87	
			p-value WRS[3]	0.1082	
Female	Baseline	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	75.44 (28.421)	53.75 (23.200)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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VABS-II Daily Living Skills Domain Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	8 (88.89)	3 (75.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (25.00)
			Mean (SD)	77.75 (25.110)	64.33 (41.405)
		Change from Baseline	n (%)	8 (88.89)	3 (75.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	-1.41 (3.415)	9.51 (5.503)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-10.92 (6.631)	
			95% CI for LS Mean Difference [2]	-25.44, 3.60	
			p-value MMRM [2]	0.1267	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-1.01	
			95% CI for SMD (Hedges' g)	-2.41, 0.40	
			p-value WRS[3]	0.1152	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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VABS-II Daily Living Skills Domain Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	71.22 (25.767)	60.50 (31.032)
		Change from Baseline	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-4.03 (3.030)	6.12 (4.814)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-10.15 (5.856)	
			95% CI for LS Mean Difference [2]	-23.19, 2.90	
			p-value MMRM [2]	0.1138	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.97	
			95% CI for SMD (Hedges' g)	-2.21, 0.28	
			p-value WRS[3]	0.0573	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.8.18 VABS-II Daily Living Skills Domain Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.4979	
<10.5 years old at screening	Baseline	Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	78.27 (22.883)	58.25 (27.909)
	Week 12	Absolute value	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	78.70 (20.913)	60.25 (30.115)
		Change from Baseline	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-0.47 (1.611)	0.83 (2.664)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.30 (3.221)	
			95% CI for LS Mean Difference [2]	-8.34, 5.73	
			p-value MMRM [2]	0.6929	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.23	
			95% CI for SMD (Hedges' g)	-1.39, 0.94	
			p-value WRS[3]	0.3477	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

NOTE: Median age used as cut-off point.

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VABS-II Daily Living Skills Domain Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	75.73 (21.143)	53.00 (26.319)
		Change from Baseline	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-2.16 (2.053)	-6.42 (3.490)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	4.26 (4.118)	
			95% CI for LS Mean Difference [2]	-4.62, 13.13	
			p-value MMRM [2]	0.3196	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.56	
			95% CI for SMD (Hedges' g)	-0.60, 1.73	
			p-value WRS[3]	0.4249	
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	64.44 (23.066)	63.14 (17.516)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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VABS-II Daily Living Skills Domain Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	8 (88.89)	5 (71.43)
			Number of patients with missing data: n (%)	1 (11.11)	2 (28.57)
			Mean (SD)	71.13 (28.063)	77.60 (20.367)
		Change from Baseline	n (%)	8 (88.89)	5 (71.43)
			Number of patients with missing data: n (%)	1 (11.11)	2 (28.57)
			LS Mean Change from Baseline (SE) [2]	3.56 (3.781)	9.97 (4.473)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-6.41 (5.854)	
			95% CI for LS Mean Difference [2]	-18.95, 6.14	
			p-value MMRM [2]	0.2920	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.56	
			95% CI for SMD (Hedges' g)	-1.70, 0.58	
			p-value WRS[3]	0.1810	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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VABS-II Daily Living Skills Domain Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	65.11 (25.551)	64.86 (19.230)
		Change from Baseline	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.68 (3.256)	1.74 (3.701)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.06 (4.922)	
			95% CI for LS Mean Difference [2]	-11.70, 9.57	
			p-value MMRM [2]	0.8322	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.10	
			95% CI for SMD (Hedges' g)	-1.09, 0.89	
			p-value WRS[3]	0.9411	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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4.10.8.19 VABS-II Daily Living Skills Domain Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.3238	
US	Baseline	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	81.25 (8.498)	66.33 (19.222)
	Week 12	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	82.13 (8.741)	70.33 (16.120)
		Change from Baseline	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	1.89 (1.718)	2.65 (2.028)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.77 (2.852)	
			95% CI for LS Mean Difference [2]	-7.03, 5.50	
			p-value MMRM [2]	0.7927	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.14	
			95% CI for SMD (Hedges' g)	-1.20, 0.92	
			p-value WRS[3]	0.3160	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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VABS-II Daily Living Skills Domain Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	81.00 (9.725)	63.17 (17.904)
		Change from Baseline	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.76 (2.091)	-4.51 (2.451)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	5.27 (3.384)	
			95% CI for LS Mean Difference [2]	-2.06, 12.61	
			p-value MMRM [2]	0.1440	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.80	
			95% CI for SMD (Hedges' g)	-0.31, 1.90	
			p-value WRS[3]	0.4332	
Non-US	Baseline	Absolute value	n (%)	12 (92.31)	5 (100.00)
			Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
			Mean (SD)	65.92 (28.292)	55.40 (22.722)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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VABS-II Daily Living Skills Domain Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	10 (76.92)	3 (60.00)
			Number of patients with missing data: n (%)	3 (23.08)	2 (40.00)
			Mean (SD)	69.90 (30.741)	69.00 (43.278)
		Change from Baseline	n (%)	10 (76.92)	3 (60.00)
			Number of patients with missing data: n (%)	3 (23.08)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	1.76 (3.502)	10.84 (5.933)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-9.09 (6.921)	
			95% CI for LS Mean Difference [2]	-23.79, 5.62	
			p-value MMRM [2]	0.2083	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.76	
			95% CI for SMD (Hedges' g)	-2.09, 0.57	
			p-value WRS[3]	0.1259	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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VABS-II Daily Living Skills Domain Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	12 (92.31)	5 (100.00)
			Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
			Mean (SD)	64.25 (27.373)	57.40 (27.208)
		Change from Baseline	n (%)	12 (92.31)	5 (100.00)
			Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-1.60 (3.062)	1.66 (4.826)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-3.26 (5.747)	
			95% CI for LS Mean Difference [2]	-15.58, 9.07	
			p-value MMRM [2]	0.5799	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.28	
			95% CI for SMD (Hedges' g)	-1.33, 0.77	
			p-value WRS[3]	0.8592	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.8.20 VABS-II Daily Living Skills Domain Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.3594	
I	Baseline	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	86.38 (13.179)	73.00 (12.083)
	Week 12	Absolute value	n (%)	8 (88.89)	4 (80.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (20.00)
			Mean (SD)	90.13 (13.778)	87.25 (13.326)
		Change from Baseline	n (%)	8 (88.89)	4 (80.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	5.25 (4.290)	6.41 (5.936)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.15 (7.676)	
			95% CI for LS Mean Difference [2]	-18.11, 15.81	
			p-value MMRM [2]	0.8834	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.08	
			95% CI for SMD (Hedges' g)	-1.29, 1.12	
			p-value WRS[3]	0.2909	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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VABS-II Daily Living Skills Domain Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	86.25 (12.045)	77.20 (13.971)
		Change from Baseline	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	1.38 (3.806)	0.89 (5.204)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.49 (6.845)	
			95% CI for LS Mean Difference [2]	-14.77, 15.74	
			p-value MMRM [2]	0.9447	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.04	
			95% CI for SMD (Hedges' g)	-1.08, 1.16	
			p-value WRS[3]	0.8625	
≥ II	Baseline	Absolute value	n (%)	12 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	62.50 (24.284)	51.67 (21.970)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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VABS-II Daily Living Skills Domain Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	10 (83.33)	5 (83.33)
			Number of patients with missing data: n (%)	2 (16.67)	1 (16.67)
			Mean (SD)	63.50 (24.094)	56.00 (24.218)
		Change from Baseline	n (%)	10 (83.33)	5 (83.33)
			Number of patients with missing data: n (%)	2 (16.67)	1 (16.67)
			LS Mean Change from Baseline (SE) [2]	-0.46 (1.684)	3.66 (2.396)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-4.12 (2.959)	
			95% CI for LS Mean Difference [2]	-10.46, 2.22	
			p-value MMRM [2]	0.1853	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.71	
			95% CI for SMD (Hedges' g)	-1.81, 0.40	
			p-value WRS[3]	0.1705	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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VABS-II Daily Living Skills Domain Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	12 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	60.75 (23.576)	46.67 (16.318)
		Change from Baseline	n (%)	12 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-1.47 (1.515)	-5.74 (2.170)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	4.26 (2.669)	
			95% CI for LS Mean Difference [2]	-1.41, 9.94	
			p-value MMRM [2]	0.1305	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.75	
			95% CI for SMD (Hedges' g)	-0.27, 1.76	
			p-value WRS[3]	0.3674	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.8.21 VABS-II Daily Living Skills Domain Score responders ≥ 7,5 by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Gender, p-value Chi-Square[1]	0.9536	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (14.29)
		Non-Responders [2]	10 (83.33)	6 (85.71)
		Responders	2 (16.67)	1 (14.29)
		OR (95% CI)	1.20 (0.09, 16.24)	
		RR (95% CI)	1.17 (0.13, 10.66)	
		RD % (95% CI)	2.38 (-31.03, 35.80)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [2]	10 (83.33)	7 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	3.57 (0.15, 85.68)	
		RR (95% CI)	3.08 (0.17, 56.25)	
		RD % (95% CI)	12.98 (-14.23, 40.19)	
		p-value – Fisher's Exact Test	0.5088	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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VABS-II Daily Living Skills Domain Score responders ≥ 7,5 by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (25.00)
		Non-Responders [2]	9 (100.00)	3 (75.00)
		Responders	0 (0.00)	1 (25.00)
		OR (95% CI)	0.12 (0.00, 3.78)	
		RR (95% CI)	0.17 (0.01, 3.40)	
		RD % (95% CI)	-25.00 (-67.38, 17.38)	
		p-value – Fisher's Exact Test	0.3077	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	9 (100.00)	3 (75.00)
		Responders	0 (0.00)	1 (25.00)
		OR (95% CI)	0.12 (0.00, 3.78)	
		RR (95% CI)	0.17 (0.01, 3.40)	
		RD % (95% CI)	-25.00 (-67.38, 17.38)	
		p-value – Fisher's Exact Test	0.3077	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.8.22 VABS-II Daily Living Skills Domain Score responders ≥ 7,5 by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Age Group, p-value Chi-Square[1]	0.9781	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	12 (100.00)	4 (100.00)
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [2]	11 (91.67)	4 (100.00)
		Responders	1 (8.33)	0 (0.00)
		OR (95% CI)	1.17 (0.04, 34.52)	
		RR (95% CI)	1.15 (0.06, 23.88)	
		RD % (95% CI)	1.54 (-29.97, 33.05)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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VABS-II Daily Living Skills Domain Score responders ≥ 7,5 by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	2 (28.57)
		Non-Responders [2]	7 (77.78)	5 (71.43)
		Responders	2 (22.22)	2 (28.57)
		OR (95% CI)	0.71 (0.07, 6.92)	
		RR (95% CI)	0.78 (0.14, 4.23)	
		RD % (95% CI)	-6.35 (-49.45, 36.75)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	8 (88.89)	6 (85.71)
		Responders	1 (11.11)	1 (14.29)
		OR (95% CI)	0.75 (0.04, 14.58)	
		RR (95% CI)	0.78 (0.06, 10.37)	
		RD % (95% CI)	-3.17 (-36.24, 29.89)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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4.10.8.23 VABS-II Daily Living Skills Domain Score responders ≥ 7,5 by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Region, p-value Chi-Square[1]	0.9701	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	7 (87.50)	5 (83.33)
		Responders	1 (12.50)	1 (16.67)
		OR (95% CI)	0.71 (0.04, 14.35)	
		RR (95% CI)	0.75 (0.06, 9.72)	
		RD % (95% CI)	-4.17 (-41.78, 33.44)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	7 (87.50)	6 (100.00)
		Responders	1 (12.50)	0 (0.00)
		OR (95% CI)	2.60 (0.09, 75.49)	
		RR (95% CI)	2.33 (0.11, 48.99)	
		RD % (95% CI)	9.52 (-21.41, 40.46)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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VABS-II Daily Living Skills Domain Score responders ≥ 7,5 by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (23.08)	2 (40.00)
		Non-Responders [2]	12 (92.31)	4 (80.00)
		Responders	1 (7.69)	1 (20.00)
		OR (95% CI)	0.33 (0.02, 6.65)	
		RR (95% CI)	0.38 (0.03, 5.04)	
		RD % (95% CI)	-12.31 (-50.24, 25.63)	
		p-value – Fisher's Exact Test	0.4902	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (7.69)	0 (0.00)
		Non-Responders [2]	12 (92.31)	4 (80.00)
		Responders	1 (7.69)	1 (20.00)
		OR (95% CI)	0.33 (0.02, 6.65)	
		RR (95% CI)	0.38 (0.03, 5.04)	
		RD % (95% CI)	-12.31 (-50.24, 25.63)	
		p-value – Fisher's Exact Test	0.4902	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.8.24 VABS-II Daily Living Skills Domain Score responders ≥ 7,5 by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.9997	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (20.00)
		Non-Responders [2]	7 (77.78)	4 (80.00)
		Responders	2 (22.22)	1 (20.00)
		OR (95% CI)	1.14 (0.08, 16.95)	
		RR (95% CI)	1.11 (0.13, 9.42)	
		RD % (95% CI)	2.22 (-42.13, 46.57)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	7 (77.78)	4 (80.00)
		Responders	2 (22.22)	1 (20.00)
		OR (95% CI)	1.14 (0.08, 16.95)	
		RR (95% CI)	1.11 (0.13, 9.42)	
		RD % (95% CI)	2.22 (-42.13, 46.57)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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VABS-II Daily Living Skills Domain Score responders ≥ 7,5 by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (16.67)
		Non-Responders [2]	12 (100.00)	5 (83.33)
		Responders	0 (0.00)	1 (16.67)
		OR (95% CI)	0.15 (0.01, 4.20)	
		RR (95% CI)	0.18 (0.01, 3.85)	
		RD % (95% CI)	-17.58 (-49.73, 14.56)	
		p-value – Fisher's Exact Test	0.3333	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	12 (100.00)	6 (100.00)

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-sub.sas
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4.10.8.25 VABS-II Socialization Domain Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.6475	
Male	Baseline	Absolute value	n (%)	11 (91.67)	7 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	82.45 (20.791)	68.71 (12.338)
	Week 12	Absolute value	n (%)	10 (83.33)	6 (85.71)
			Number of patients with missing data: n (%)	2 (16.67)	1 (14.29)
			Mean (SD)	75.50 (20.748)	75.50 (19.295)
		Change from Baseline	n (%)	10 (83.33)	6 (85.71)
			Number of patients with missing data: n (%)	2 (16.67)	1 (14.29)
			LS Mean Change from Baseline (SE) [2]	-6.67 (3.915)	4.55 (5.091)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-11.22 (6.581)	
			95% CI for LS Mean Difference [2]	-25.22, 2.78	
			p-value MMRM [2]	0.1083	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.83	
			95% CI for SMD (Hedges' g)	-1.89, 0.23	
			p-value WRS[3]	0.0516	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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VABS-II Socialization Domain Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	11 (91.67)	7 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	78.73 (21.882)	65.29 (10.144)
		Change from Baseline	n (%)	11 (91.67)	7 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-2.84 (3.676)	-5.06 (4.711)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.22 (6.135)	
			95% CI for LS Mean Difference [2]	-10.77, 15.22	
			p-value MMRM [2]	0.7220	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.17	
			95% CI for SMD (Hedges' g)	-0.78, 1.12	
			p-value WRS[3]	0.9119	
Female	Baseline	Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	83.38 (29.713)	50.25 (25.356)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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VABS-II Socialization Domain Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	8 (88.89)	3 (75.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (25.00)
			Mean (SD)	81.88 (28.503)	57.33 (32.332)
		Change from Baseline	n (%)	8 (88.89)	3 (75.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	0.74 (5.428)	4.31 (8.218)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-3.58 (10.110)	
			95% CI for LS Mean Difference [2]	-25.67, 18.52	
			p-value MMRM [2]	0.7299	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.21	
			95% CI for SMD (Hedges' g)	-1.54, 1.12	
			p-value WRS[3]	0.6364	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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VABS-II Socialization Domain Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	75.56 (23.511)	55.75 (24.295)
		Change from Baseline	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-4.26 (3.600)	0.41 (5.438)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-4.67 (6.911)	
			95% CI for LS Mean Difference [2]	-20.10, 10.76	
			p-value MMRM [2]	0.5148	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.39	
			95% CI for SMD (Hedges' g)	-1.61, 0.82	
			p-value WRS[3]	0.2101	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.8.26 VABS-II Socialization Domain Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.6048	
<10.5 years old at screening	Baseline	Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	86.73 (21.247)	57.75 (26.725)
	Week 12	Absolute value	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	82.70 (24.157)	57.50 (27.982)
		Change from Baseline	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-3.30 (4.547)	-3.63 (7.444)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.33 (8.909)	
			95% CI for LS Mean Difference [2]	-18.79, 19.46	
			p-value MMRM [2]	0.9706	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.02	
			95% CI for SMD (Hedges' g)	-1.14, 1.18	
			p-value WRS[3]	0.5594	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

NOTE: Median age used as cut-off point.

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VABS-II Socialization Domain Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	79.09 (18.014)	55.75 (26.800)
		Change from Baseline	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-6.45 (2.405)	-5.38 (4.354)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.07 (5.289)	
			95% CI for LS Mean Difference [2]	-12.59, 10.46	
			p-value MMRM [2]	0.8436	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.12	
			95% CI for SMD (Hedges' g)	-1.26, 1.03	
			p-value WRS[3]	0.3231	
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	8 (88.89)	7 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	77.50 (28.279)	64.43 (15.566)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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VABS-II Socialization Domain Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	8 (88.89)	5 (71.43)
			Number of patients with missing data: n (%)	1 (11.11)	2 (28.57)
			Mean (SD)	72.88 (24.086)	79.00 (17.578)
		Change from Baseline	n (%)	8 (88.89)	5 (71.43)
			Number of patients with missing data: n (%)	1 (11.11)	2 (28.57)
			LS Mean Change from Baseline (SE) [2]	-3.32 (4.085)	10.79 (4.880)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-14.11 (6.474)	
			95% CI for LS Mean Difference [2]	-28.19, -0.03	
			p-value MMRM [2]	0.0496 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-1.12	
			95% CI for SMD (Hedges' g)	-2.33, 0.09	
			p-value WRS[3]	0.0598	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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VABS-II Socialization Domain Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	75.11 (27.242)	65.29 (6.237)
		Change from Baseline	n (%)	8 (88.89)	7 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.18 (4.855)	-1.18 (5.257)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.36 (7.273)	
			95% CI for LS Mean Difference [2]	-14.36, 17.08	
			p-value MMRM [2]	0.8543	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.09	
			95% CI for SMD (Hedges' g)	-0.93, 1.10	
			p-value WRS[3]	0.9363	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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4.10.8.27 VABS-II Socialization Domain Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.1766	
US	Baseline	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	91.50 (14.599)	69.17 (12.906)
	Week 12	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	91.38 (13.897)	70.17 (11.268)
		Change from Baseline	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	3.35 (3.528)	-3.63 (4.152)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	6.97 (5.791)	
			95% CI for LS Mean Difference [2]	-5.38, 19.33	
			p-value MMRM [2]	0.2473	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.63	
			95% CI for SMD (Hedges' g)	-0.46, 1.72	
			p-value WRS[3]	0.6370	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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VABS-II Socialization Domain Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	84.88 (10.077)	65.50 (10.766)
		Change from Baseline	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-3.15 (2.317)	-8.29 (2.793)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	5.14 (4.126)	
			95% CI for LS Mean Difference [2]	-3.94, 14.22	
			p-value MMRM [2]	0.2386	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.69	
			95% CI for SMD (Hedges' g)	-0.41, 1.78	
			p-value WRS[3]	0.6836	
Non-US	Baseline	Absolute value	n (%)	11 (84.62)	5 (100.00)
			Number of patients with missing data: n (%)	2 (15.38)	0 (0.00)
			Mean (SD)	76.55 (28.247)	53.40 (23.448)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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VABS-II Socialization Domain Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	10 (76.92)	3 (60.00)
			Number of patients with missing data: n (%)	3 (23.08)	2 (40.00)
			Mean (SD)	67.90 (25.692)	68.00 (44.542)
		Change from Baseline	n (%)	10 (76.92)	3 (60.00)
			Number of patients with missing data: n (%)	3 (23.08)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-7.67 (4.527)	14.63 (8.197)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-22.30 (9.594)	
			95% CI for LS Mean Difference [2]	-42.90, -1.71	
			p-value MMRM [2]	0.0358 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-1.41	
			95% CI for SMD (Hedges' g)	-2.83, 0.01	
			p-value WRS[3]	0.0315 ***	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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VABS-II Socialization Domain Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	12 (92.31)	5 (100.00)
			Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
			Mean (SD)	72.25 (26.602)	57.40 (21.571)
		Change from Baseline	n (%)	11 (84.62)	5 (100.00)
			Number of patients with missing data: n (%)	2 (15.38)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-2.64 (4.384)	1.48 (6.747)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-4.13 (8.285)	
			95% CI for LS Mean Difference [2]	-21.90, 13.65	
			p-value MMRM [2]	0.6261	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.26	
			95% CI for SMD (Hedges' g)	-1.32, 0.81	
			p-value WRS[3]	0.4398	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.8.28 VABS-II Socialization Domain Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.9857	
I	Baseline	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	90.00 (16.248)	67.40 (16.832)
	Week 12	Absolute value	n (%)	8 (88.89)	4 (80.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (20.00)
			Mean (SD)	87.13 (11.064)	78.50 (5.686)
		Change from Baseline	n (%)	8 (88.89)	4 (80.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	1.81 (3.129)	-0.19 (4.457)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.00 (5.911)	
			95% CI for LS Mean Difference [2]	-11.23, 15.23	
			p-value MMRM [2]	0.7423	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.20	
			95% CI for SMD (Hedges' g)	-1.01, 1.40	
			p-value WRS[3]	0.4606	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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VABS-II Socialization Domain Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	87.63 (16.535)	70.00 (9.644)
		Change from Baseline	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	2.31 (4.492)	-6.86 (6.021)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	9.17 (7.929)	
			95% CI for LS Mean Difference [2]	-8.04, 26.38	
			p-value MMRM [2]	0.2691	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.63	
			95% CI for SMD (Hedges' g)	-0.52, 1.78	
			p-value WRS[3]	0.6939	
≥ II	Baseline	Absolute value	n (%)	11 (91.67)	6 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	77.64 (28.197)	57.50 (21.492)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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VABS-II Socialization Domain Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	10 (83.33)	5 (83.33)
			Number of patients with missing data: n (%)	2 (16.67)	1 (16.67)
			Mean (SD)	71.30 (29.387)	62.20 (31.324)
		Change from Baseline	n (%)	10 (83.33)	5 (83.33)
			Number of patients with missing data: n (%)	2 (16.67)	1 (16.67)
			LS Mean Change from Baseline (SE) [2]	-4.79 (4.786)	3.50 (6.802)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-8.29 (8.410)	
			95% CI for LS Mean Difference [2]	-26.29, 9.71	
			p-value MMRM [2]	0.3407	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.50	
			95% CI for SMD (Hedges' g)	-1.59, 0.59	
			p-value WRS[3]	0.0896	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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VABS-II Socialization Domain Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	12 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	70.42 (23.208)	55.00 (18.078)
		Change from Baseline	n (%)	11 (91.67)	6 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-5.39 (2.663)	-5.01 (3.698)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.38 (4.718)	
			95% CI for LS Mean Difference [2]	-10.49, 9.73	
			p-value MMRM [2]	0.9367	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.04	
			95% CI for SMD (Hedges' g)	-1.03, 0.96	
			p-value WRS[3]	0.8256	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.8.29 VABS-II Socialization Domain Score responders ≥ 7,5 by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Gender, p-value Chi-Square[1]	0.9727	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (14.29)
		Non-Responders [2]	11 (91.67)	5 (71.43)
		Responders	1 (8.33)	2 (28.57)
		OR (95% CI)	0.23 (0.02, 3.13)	
		RR (95% CI)	0.29 (0.03, 2.66)	
		RD % (95% CI)	-20.24 (-57.18, 16.70)	
		p-value – Fisher's Exact Test	0.5232	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [2]	11 (91.67)	6 (85.71)
		Responders	1 (8.33)	1 (14.29)
		OR (95% CI)	0.55 (0.03, 10.37)	
		RR (95% CI)	0.58 (0.04, 7.94)	
		RD % (95% CI)	-5.95 (-36.23, 24.32)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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VABS-II Socialization Domain Score responders ≥ 7,5 by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (25.00)
		Non-Responders [2]	8 (88.89)	3 (75.00)
		Responders	1 (11.11)	1 (25.00)
		OR (95% CI)	0.38 (0.02, 8.10)	
		RR (95% CI)	0.44 (0.04, 5.46)	
		RD % (95% CI)	-13.89 (-61.03, 33.25)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	9 (100.00)	2 (50.00)
		Responders	0 (0.00)	2 (50.00)
		OR (95% CI)	0.05 (0.00, 1.49)	
		RR (95% CI)	0.10 (0.01, 1.71)	
		RD % (95% CI)	-45.00 (-90.86, 0.86)	
		p-value – Fisher's Exact Test	0.0769	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.8.30 VABS-II Socialization Domain Score responders ≥ 7,5 by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Age Group, p-value Chi-Square[1]	0.9966	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	11 (91.67)	4 (100.00)
		Responders	1 (8.33)	0 (0.00)
		OR (95% CI)	1.17 (0.04, 34.52)	
		RR (95% CI)	1.15 (0.06, 23.88)	
		RD % (95% CI)	1.54 (-29.97, 33.05)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [2]	12 (100.00)	4 (100.00)

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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VABS-II Socialization Domain Score responders ≥ 7,5 by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	2 (28.57)
		Non-Responders [2]	8 (88.89)	4 (57.14)
		Responders	1 (11.11)	3 (42.86)
		OR (95% CI)	0.17 (0.01, 2.16)	
		RR (95% CI)	0.26 (0.03, 1.99)	
		RD % (95% CI)	-31.75 (-73.76, 10.27)	
		p-value – Fisher's Exact Test	0.2615	
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	8 (88.89)	4 (57.14)
		Responders	1 (11.11)	3 (42.86)
		OR (95% CI)	0.17 (0.01, 2.16)	
		RR (95% CI)	0.26 (0.03, 1.99)	
		RD % (95% CI)	-31.75 (-73.76, 10.27)	
		p-value – Fisher's Exact Test	0.2615	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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4.10.8.31 VABS-II Socialization Domain Score responders ≥ 7,5 by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Region, p-value Chi-Square[1]	0.9801	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	7 (87.50)	5 (83.33)
		Responders	1 (12.50)	1 (16.67)
		OR (95% CI)	0.71 (0.04, 14.35)	
		RR (95% CI)	0.75 (0.06, 9.72)	
		RD % (95% CI)	-4.17 (-41.78, 33.44)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	8 (100.00)	5 (83.33)
		Responders	0 (0.00)	1 (16.67)
		OR (95% CI)	0.22 (0.01, 6.31)	
		RR (95% CI)	0.26 (0.01, 5.44)	
		RD % (95% CI)	-15.87 (-49.75, 18.01)	
		p-value – Fisher's Exact Test	0.4286	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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VABS-II Socialization Domain Score responders ≥ 7,5 by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (23.08)	2 (40.00)
		Non-Responders [2]	12 (92.31)	3 (60.00)
		Responders	1 (7.69)	2 (40.00)
		OR (95% CI)	0.13 (0.01, 1.89)	
		RR (95% CI)	0.19 (0.02, 1.68)	
		RD % (95% CI)	-32.31 (-77.63, 13.01)	
		p-value – Fisher's Exact Test	0.1716	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (15.38)	0 (0.00)
		Non-Responders [2]	12 (92.31)	3 (60.00)
		Responders	1 (7.69)	2 (40.00)
		OR (95% CI)	0.13 (0.01, 1.89)	
		RR (95% CI)	0.19 (0.02, 1.68)	
		RD % (95% CI)	-32.31 (-77.63, 13.01)	
		p-value – Fisher's Exact Test	0.1716	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.8.32 VABS-II Socialization Domain Score responders ≥ 7,5 by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.9747	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (20.00)
		Non-Responders [2]	8 (88.89)	4 (80.00)
		Responders	1 (11.11)	1 (20.00)
		OR (95% CI)	0.50 (0.02, 10.25)	
		RR (95% CI)	0.56 (0.04, 7.09)	
		RD % (95% CI)	-8.89 (-49.52, 31.74)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	8 (88.89)	3 (60.00)
		Responders	1 (11.11)	2 (40.00)
		OR (95% CI)	0.19 (0.01, 2.91)	
		RR (95% CI)	0.28 (0.03, 2.35)	
		RD % (95% CI)	-28.89 (-76.49, 18.71)	
		p-value – Fisher's Exact Test	0.5055	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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VABS-II Socialization Domain Score responders ≥ 7,5 by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (16.67)
		Non-Responders [2]	11 (91.67)	4 (66.67)
		Responders	1 (8.33)	2 (33.33)
		OR (95% CI)	0.18 (0.01, 2.60)	
		RR (95% CI)	0.25 (0.03, 2.24)	
		RD % (95% CI)	-25.00 (-65.83, 15.83)	
		p-value – Fisher's Exact Test	0.2451	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [2]	12 (100.00)	5 (83.33)
		Responders	0 (0.00)	1 (16.67)
		OR (95% CI)	0.15 (0.01, 4.20)	
		RR (95% CI)	0.18 (0.01, 3.85)	
		RD % (95% CI)	-17.58 (-49.73, 14.56)	
		p-value – Fisher's Exact Test	0.3333	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.8.33 VABS-II Motor Skills Domain Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	Not applicable	
Male	Baseline	Absolute value	n (%)	4 (33.33)	4 (57.14)
			Number of patients with missing data: n (%)	8 (66.67)	3 (42.86)
			Mean (SD)	37.25 (46.371)	71.00 (11.662)
	Week 12	Absolute value	n (%)	2 (16.67)	2 (28.57)
			Number of patients with missing data: n (%)	10 (83.33)	5 (71.43)
			Mean (SD)	57.50 (51.619)	62.50 (2.121)
		Change from Baseline	n (%)	2 (16.67)	2 (28.57)
			Number of patients with missing data: n (%)	10 (83.33)	5 (71.43)
			LS Mean Change from Baseline (SE) [2]	37.54 (40.981)	19.13 (39.906)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	18.41 (59.015)	
			95% CI for LS Mean Difference [2]	-169.39, 206.21	
			p-value MMRM [2]	0.7755	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.20	
			95% CI for SMD (Hedges' g)	-1.77, 2.17	
			p-value WRS[3]	0.3333	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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VABS-II Motor Skills Domain Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	3 (25.00)	2 (28.57)
			Number of patients with missing data: n (%)	9 (75.00)	5 (71.43)
			Mean (SD)	99.67 (82.646)	76.50 (24.749)
		Change from Baseline	n (%)	3 (25.00)	2 (28.57)
			Number of patients with missing data: n (%)	9 (75.00)	5 (71.43)
			LS Mean Change from Baseline (SE) [2]	37.04 (40.980)	17.13 (39.906)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	19.91 (59.015)	
			95% CI for LS Mean Difference [2]	-167.89, 207.71	
			p-value MMRM [2]	0.7580	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.18	
			95% CI for SMD (Hedges' g)	-1.61, 1.98	
			p-value WRS[3]	0.8000	
Female	Baseline	Absolute value	n (%)	5 (55.56)	1 (25.00)
			Number of patients with missing data: n (%)	4 (44.44)	3 (75.00)
			Mean (SD)	81.20 (11.167)	195.00 (-)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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VABS-II Motor Skills Domain Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	4 (44.44)	0 (0.00)
			Number of patients with missing data: n (%)	5 (55.56)	4 (100.00)
			Mean (SD)	79.75 (13.276)	- (-)
		Change from Baseline	n (%)	4 (44.44)	0 (0.00)
			Number of patients with missing data: n (%)	5 (55.56)	4 (100.00)
			LS Mean Change from Baseline (SE) [2]	-3.00 (4.068)	- (-)
	Week 24	Absolute value	n (%)	5 (55.56)	0 (0.00)
			Number of patients with missing data: n (%)	4 (44.44)	4 (100.00)
			Mean (SD)	73.40 (13.502)	- (-)
		Change from Baseline	n (%)	4 (44.44)	0 (0.00)
			Number of patients with missing data: n (%)	5 (55.56)	4 (100.00)
			LS Mean Change from Baseline (SE) [2]	-4.75 (4.068)	- (-)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.8.34 VABS-II Motor Skills Domain Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	Not applicable	
<10.5 years old at screening	Baseline	Absolute value	n (%)	8 (66.67)	3 (75.00)
			Number of patients with missing data: n (%)	4 (33.33)	1 (25.00)
			Mean (SD)	69.38 (31.541)	67.67 (11.719)
	Week 12	Absolute value	n (%)	6 (50.00)	2 (50.00)
			Number of patients with missing data: n (%)	6 (50.00)	2 (50.00)
			Mean (SD)	72.33 (27.761)	62.50 (2.121)
		Change from Baseline	n (%)	6 (50.00)	2 (50.00)
			Number of patients with missing data: n (%)	6 (50.00)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	-4.20 (2.026)	1.98 (3.736)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-6.18 (4.311)	
			95% CI for LS Mean Difference [2]	-17.01, 4.64	
			p-value MMRM [2]	0.2065	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.94	
			95% CI for SMD (Hedges' g)	-2.62, 0.75	
			p-value WRS[3]	0.2143	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

NOTE: Median age used as cut-off point.

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VABS-II Motor Skills Domain Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	6 (50.00)	2 (50.00)
			Number of patients with missing data: n (%)	6 (50.00)	2 (50.00)
			Mean (SD)	71.00 (26.952)	76.50 (24.749)
		Change from Baseline	n (%)	6 (50.00)	2 (50.00)
			Number of patients with missing data: n (%)	6 (50.00)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	-5.54 (3.310)	5.75 (5.826)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-11.29 (6.710)	
			95% CI for LS Mean Difference [2]	-27.40, 4.83	
			p-value MMRM [2]	0.1396	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-1.12	
			95% CI for SMD (Hedges' g)	-2.84, 0.60	
			p-value WRS[3]	0.1429	
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	1 (11.11)	2 (28.57)
			Number of patients with missing data: n (%)	8 (88.89)	5 (71.43)
			Mean (SD)	0.00 (-)	138.00 (80.610)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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VABS-II Motor Skills Domain Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	0 (0.00)	0 (0.00)
			Number of patients with missing data: n (%)	9 (100.00)	7 (100.00)
			Mean (SD)	- (-)	- (-)
		Change from Baseline	n (%)	0 (0.00)	0 (0.00)
			Number of patients with missing data: n (%)	9 (100.00)	7 (100.00)
	Week 24	Absolute value	n (%)	2 (22.22)	0 (0.00)
			Number of patients with missing data: n (%)	7 (77.78)	7 (100.00)
			Mean (SD)	120.00 (91.924)	- (-)
		Change from Baseline	n (%)	1 (11.11)	0 (0.00)
			Number of patients with missing data: n (%)	8 (88.89)	7 (100.00)
			LS Mean Change from Baseline (SE) [2]	185.00 (0.000)	- (-)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
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4.10.8.35 VABS-II Motor Skills Domain Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	Not applicable	
US	Baseline	Absolute value	n (%)	6 (75.00)	4 (66.67)
			Number of patients with missing data: n (%)	2 (25.00)	2 (33.33)
			Mean (SD)	73.50 (37.888)	71.00 (11.662)
	Week 12	Absolute value	n (%)	4 (50.00)	2 (33.33)
			Number of patients with missing data: n (%)	4 (50.00)	4 (66.67)
			Mean (SD)	86.50 (11.358)	62.50 (2.121)
		Change from Baseline	n (%)	4 (50.00)	2 (33.33)
			Number of patients with missing data: n (%)	4 (50.00)	4 (66.67)
			LS Mean Change from Baseline (SE) [2]	27.45 (13.231)	-8.25 (17.808)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	35.70 (21.904)	
			95% CI for LS Mean Difference [2]	-25.18, 96.58	
			p-value MMRM [2]	0.1787	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.94	
			95% CI for SMD (Hedges' g)	-0.88, 2.76	
			p-value WRS[3]	0.5333	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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VABS-II Motor Skills Domain Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	5 (62.50)	2 (33.33)
			Number of patients with missing data: n (%)	3 (37.50)	4 (66.67)
			Mean (SD)	105.40 (44.892)	76.50 (24.749)
		Change from Baseline	n (%)	5 (62.50)	2 (33.33)
			Number of patients with missing data: n (%)	3 (37.50)	4 (66.67)
			LS Mean Change from Baseline (SE) [2]	25.94 (10.723)	-12.48 (14.699)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	38.42 (18.059)	
			95% CI for LS Mean Difference [2]	-7.52, 84.37	
			p-value MMRM [2]	0.0847	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.25	
			95% CI for SMD (Hedges' g)	-0.56, 3.07	
			p-value WRS[3]	0.5714	
Non-US	Baseline	Absolute value	n (%)	3 (23.08)	1 (20.00)
			Number of patients with missing data: n (%)	10 (76.92)	4 (80.00)
			Mean (SD)	38.00 (27.785)	195.00 (-)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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VABS-II Motor Skills Domain Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	2 (15.38)	0 (0.00)
			Number of patients with missing data: n (%)	11 (84.62)	5 (100.00)
			Mean (SD)	44.00 (32.527)	- (-)
		Change from Baseline	n (%)	2 (15.38)	0 (0.00)
			Number of patients with missing data: n (%)	11 (84.62)	5 (100.00)
	Week 24	Absolute value	n (%)	3 (23.08)	0 (0.00)
			Number of patients with missing data: n (%)	10 (76.92)	5 (100.00)
			Mean (SD)	46.33 (23.245)	- (-)
		Change from Baseline	n (%)	2 (15.38)	0 (0.00)
			Number of patients with missing data: n (%)	11 (84.62)	5 (100.00)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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4.10.8.36 VABS-II Motor Skills Domain Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.6636	
I	Baseline	Absolute value	n (%)	3 (33.33)	3 (60.00)
			Number of patients with missing data: n (%)	6 (66.67)	2 (40.00)
			Mean (SD)	90.33 (18.175)	119.00 (65.818)
	Week 12	Absolute value	n (%)	3 (33.33)	0 (0.00)
			Number of patients with missing data: n (%)	6 (66.67)	5 (100.00)
			Mean (SD)	83.00 (14.177)	- (-)
		Change from Baseline	n (%)	3 (33.33)	0 (0.00)
			Number of patients with missing data: n (%)	6 (66.67)	5 (100.00)
	Week 24	Absolute value	n (%)	3 (33.33)	1 (20.00)
			Number of patients with missing data: n (%)	6 (66.67)	4 (80.00)
			Mean (SD)	79.00 (15.000)	94.00 (-)
		Change from Baseline	n (%)	3 (33.33)	1 (20.00)
			Number of patients with missing data: n (%)	6 (66.67)	4 (80.00)
			p-value WRS[3]	0.5000	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

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VABS-II Motor Skills Domain Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Baseline	Absolute value	n (%)	6 (50.00)	2 (33.33)
			Number of patients with missing data: n (%)	6 (50.00)	4 (66.67)
			Mean (SD)	47.33 (37.103)	61.00 (2.828)
	Week 12	Absolute value	n (%)	3 (25.00)	2 (33.33)
			Number of patients with missing data: n (%)	9 (75.00)	4 (66.67)
			Mean (SD)	61.67 (37.207)	62.50 (2.121)
		Change from Baseline	n (%)	3 (25.00)	2 (33.33)
			Number of patients with missing data: n (%)	9 (75.00)	4 (66.67)
			LS Mean Change from Baseline (SE) [2]	-1.88 (3.132)	1.19 (3.016)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-3.07 (4.160)	
			95% CI for LS Mean Difference [2]	-20.98, 14.84	
			p-value MMRM [2]	0.5373	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.28	
			95% CI for SMD (Hedges' g)	-2.08, 1.53	
			p-value WRS[3]	0.8000	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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VABS-II Motor Skills Domain Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	5 (41.67)	1 (16.67)
			Number of patients with missing data: n (%)	7 (58.33)	5 (83.33)
			Mean (SD)	85.80 (61.536)	59.00 (-)
		Change from Baseline	n (%)	4 (33.33)	1 (16.67)
			Number of patients with missing data: n (%)	8 (66.67)	5 (83.33)
			LS Mean Change from Baseline (SE) [2]	46.78 (47.274)	0.61 (135.215)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	46.17 (143.233)	
			95% CI for LS Mean Difference [2]	-412.31, 504.64	
			p-value MMRM [2]	0.7686	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.30	
			95% CI for SMD (Hedges' g)	-1.90, 2.50	
			p-value WRS[3]	1.0000	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
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4.10.8.37 VABS-II Motor Skills Domain Score responders ≥ 7,5 by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Gender, p-value Chi-Square[1]	0.9987	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	10 (83.33)	5 (71.43)
		Non-Responders [2]	12 (100.00)	7 (100.00)
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	9 (75.00)	5 (71.43)
		Non-Responders [2]	11 (91.67)	6 (85.71)
		Responders	1 (8.33)	1 (14.29)
		OR (95% CI)	0.55 (0.03, 10.37)	
		RR (95% CI)	0.58 (0.04, 7.94)	
		RD % (95% CI)	-5.95 (-36.23, 24.32)	
		p-value – Fisher's Exact Test	1.0000	
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	5 (55.56)	4 (100.00)
		Non-Responders [2]	9 (100.00)	4 (100.00)

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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VABS-II Motor Skills Domain Score responders ≥ 7,5 by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	5 (55.56)	4 (100.00)
		Non-Responders [2]	9 (100.00)	4 (100.00)

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.8.38 VABS-II Motor Skills Domain Score responders ≥ 7,5 by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Age Group, p-value Chi-Square[1]	0.9378	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	6 (50.00)	2 (50.00)
		Non-Responders [2]	12 (100.00)	4 (100.00)
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	6 (50.00)	2 (50.00)
		Non-Responders [2]	12 (100.00)	3 (75.00)
		Responders	0 (0.00)	1 (25.00)
		OR (95% CI)	0.09 (0.00, 2.83)	
		RR (95% CI)	0.13 (0.01, 2.65)	
		RD % (95% CI)	-26.15 (-67.66, 15.35)	
		p-value – Fisher's Exact Test	0.2500	
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	9 (100.00)	7 (100.00)
		Non-Responders [2]	9 (100.00)	7 (100.00)

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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VABS-II Motor Skills Domain Score responders ≥ 7,5 by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	8 (88.89)	7 (100.00)
		Non-Responders [2]	8 (88.89)	7 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	2.65 (0.09, 75.29)	
		RR (95% CI)	2.40 (0.11, 51.32)	
		RD % (95% CI)	8.75 (-19.02, 36.52)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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4.10.8.39 VABS-II Motor Skills Domain Score responders ≥ 7,5 by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Region, p-value Chi-Square[1]	0.9992	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	4 (50.00)	4 (66.67)
		Non-Responders [2]	8 (100.00)	6 (100.00)
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (37.50)	4 (66.67)
		Non-Responders [2]	7 (87.50)	5 (83.33)
		Responders	1 (12.50)	1 (16.67)
		OR (95% CI)	0.71 (0.04, 14.35)	
		RR (95% CI)	0.75 (0.06, 9.72)	
		RD % (95% CI)	-4.17 (-41.78, 33.44)	
		p-value – Fisher's Exact Test	1.0000	
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	11 (84.62)	5 (100.00)
		Non-Responders [2]	13 (100.00)	5 (100.00)

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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VABS-II Motor Skills Domain Score responders ≥ 7,5 by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	11 (84.62)	5 (100.00)
		Non-Responders [2]	13 (100.00)	5 (100.00)

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.8.40 VABS-II Motor Skills Domain Score responders ≥ 7,5 by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.9454	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	6 (66.67)	5 (100.00)
		Non-Responders [2]	9 (100.00)	5 (100.00)
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	6 (66.67)	4 (80.00)
		Non-Responders [2]	9 (100.00)	4 (80.00)
		Responders	0 (0.00)	1 (20.00)
		OR (95% CI)	0.16 (0.01, 4.69)	
		RR (95% CI)	0.20 (0.01, 4.17)	
		RD % (95% CI)	-20.00 (-57.19, 17.19)	
		p-value – Fisher's Exact Test	0.3571	
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	9 (75.00)	4 (66.67)
		Non-Responders [2]	12 (100.00)	6 (100.00)

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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VABS-II Motor Skills Domain Score responders ≥ 7,5 by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	8 (66.67)	5 (83.33)
		Non-Responders [2]	11 (91.67)	6 (100.00)
		Responders	1 (8.33)	0 (0.00)
		OR (95% CI)	1.70 (0.06, 47.95)	
		RR (95% CI)	1.62 (0.08, 34.66)	
		RD % (95% CI)	4.40 (-21.40, 30.19)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.8.41 Subgruppenanalysen von Sensitivitätsanalysen für den Endpunkt VABS-II

4.10.8.42 VABS-II Adaptive Behavior Composite Score by gender (including patients where composite score was erroneously not calculated)

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Baseline	Absolute value	n (%)	11 (91.67)	7 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	69.73 (24.405)	70.43 (17.850)
	Week 12	Absolute value	n (%)	10 (83.33)	6 (85.71)
			Number of patients with missing data: n (%)	2 (16.67)	1 (14.29)
			Mean (SD)	76.60 (21.506)	74.17 (18.904)
		Change from Baseline	n (%)	10 (83.33)	6 (85.71)
			Number of patients with missing data: n (%)	2 (16.67)	1 (14.29)
			LS Mean Change from Baseline (SE) [2]	6.15 (5.315)	1.80 (6.464)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	4.35 (8.368)	
			95% CI for LS Mean Difference [2]	-13.48, 22.18	
			p-value MMRM [2]	0.6109	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.24	
			95% CI for SMD (Hedges' g)	-0.77, 1.26	
			p-value WRS[3]	0.5089	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

NOTE: Including patients where previously Adaptive Behavior Composite Score (ABCS) was erroneously not calculated (ABCS for patients 134-0002 and 146-0002 at Week 24 were calculated after data-base lock)

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1.4.16 Sensitivity analyses for VABS-II Adaptive Behavior Composite Score
VABS-II Adaptive Behavior Composite Score by gender (including patients where composite score was erroneously not calculated)

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	10 (83.33)	7 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	75.30 (19.189)	66.14 (12.628)
		Change from Baseline	n (%)	10 (83.33)	7 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	4.85 (4.029)	-4.42 (4.815)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	9.27 (6.278)	
			95% CI for LS Mean Difference [2]	-4.18, 22.72	
			p-value MMRM [2]	0.1616	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.67	
			95% CI for SMD (Hedges' g)	-0.33, 1.66	
			p-value WRS[3]	0.3012	
Female	Baseline	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	73.78 (25.543)	61.75 (7.676)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Including patients where previously Adaptive Behavior Composite Score (ABCS) was erroneously not calculated (ABCS for patients 134-0002 and 146-0002 at Week 24 were calculated after data-base lock)
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1.4.16 Sensitivity analyses for VABS-II Adaptive Behavior Composite Score
VABS-II Adaptive Behavior Composite Score by gender (including patients where composite score was erroneously not calculated)

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	8 (88.89)	3 (75.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (25.00)
			Mean (SD)	75.88 (24.649)	71.00 (10.536)
		Change from Baseline	n (%)	8 (88.89)	3 (75.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	1.79 (3.031)	5.26 (4.717)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-3.48 (5.628)	
			95% CI for LS Mean Difference [2]	-15.88, 8.93	
			p-value MMRM [2]	0.5496	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.36	
			95% CI for SMD (Hedges' g)	-1.70, 0.98	
			p-value WRS[3]	0.2606	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Including patients where previously Adaptive Behavior Composite Score (ABCS) was erroneously not calculated (ABCS for patients 134-0002 and 146-0002 at Week 24 were calculated after data-base lock)
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1.4.16 Sensitivity analyses for VABS-II Adaptive Behavior Composite Score
VABS-II Adaptive Behavior Composite Score by gender (including patients where composite score was erroneously not calculated)

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	71.00 (21.743)	65.00 (6.272)
		Change from Baseline	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-2.26 (2.272)	0.98 (3.513)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-3.23 (4.229)	
			95% CI for LS Mean Difference [2]	-12.62, 6.15	
			p-value MMRM [2]	0.4614	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.41	
			95% CI for SMD (Hedges' g)	-1.61, 0.78	
			p-value WRS[3]	0.2126	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Including patients where previously Adaptive Behavior Composite Score (ABCS) was erroneously not calculated (ABCS for patients 134-0002 and 146-0002 at Week 24 were calculated after data-base lock)
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4.10.8.43 VABS-II Adaptive Behavior Composite Score by age group (including patients where composite score was erroneously not calculated)

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Baseline	Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	75.18 (26.011)	66.25 (10.595)
	Week 12	Absolute value	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	81.30 (18.839)	66.50 (12.342)
		Change from Baseline	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	6.67 (4.920)	-3.68 (7.793)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	10.36 (9.233)	
			95% CI for LS Mean Difference [2]	-9.76, 30.47	
			p-value MMRM [2]	0.2839	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.60	
			95% CI for SMD (Hedges' g)	-0.59, 1.78	
			p-value WRS[3]	0.6124	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

NOTE: Median age used as cut-off point.

NOTE: Including patients where previously Adaptive Behavior Composite Score (ABCS) was erroneously not calculated (ABCS for patients 134-0002 and 146-0002 at Week 24 were calculated after data-base lock)

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VABS-II Adaptive Behavior Composite Score by age group (including patients where composite score was erroneously not calculated)

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	77.40 (14.645)	64.25 (11.471)
		Change from Baseline	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	2.77 (3.324)	-5.93 (5.277)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	8.71 (6.260)	
			95% CI for LS Mean Difference [2]	-4.95, 22.36	
			p-value MMRM [2]	0.1898	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.74	
			95% CI for SMD (Hedges' g)	-0.45, 1.94	
			p-value WRS[3]	0.9740	
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	67.11 (22.828)	67.86 (17.967)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
NOTE: Including patients where previously Adaptive Behavior Composite Score (ABCS) was erroneously not calculated (ABCS for patients 134-0002 and 146-0002 at Week 24 were calculated after data-base lock)
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VABS-II Adaptive Behavior Composite Score by age group (including patients where composite score was erroneously not calculated)

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	8 (88.89)	5 (71.43)
			Number of patients with missing data: n (%)	1 (11.11)	2 (28.57)
			Mean (SD)	70.00 (25.790)	78.40 (17.729)
		Change from Baseline	n (%)	8 (88.89)	5 (71.43)
			Number of patients with missing data: n (%)	1 (11.11)	2 (28.57)
			LS Mean Change from Baseline (SE) [2]	1.56 (3.087)	6.83 (3.676)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-5.27 (4.804)	
			95% CI for LS Mean Difference [2]	-15.64, 5.10	
			p-value MMRM [2]	0.2922	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.56	
			95% CI for SMD (Hedges' g)	-1.70, 0.58	
			p-value WRS[3]	0.3699	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
NOTE: Including patients where previously Adaptive Behavior Composite Score (ABCS) was erroneously not calculated (ABCS for patients 134-0002 and 146-0002 at Week 24 were calculated after data-base lock)
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VABS-II Adaptive Behavior Composite Score by age group (including patients where composite score was erroneously not calculated)

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	68.67 (24.729)	66.57 (10.565)
		Change from Baseline	n (%)	9 (100.00)	7 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	1.40 (3.408)	-1.37 (3.858)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.77 (5.143)	
			95% CI for LS Mean Difference [2]	-8.36, 13.90	
			p-value MMRM [2]	0.5988	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.25	
			95% CI for SMD (Hedges' g)	-0.75, 1.24	
			p-value WRS[3]	0.7384	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Median age used as cut-off point.
NOTE: Including patients where previously Adaptive Behavior Composite Score (ABCS) was erroneously not calculated (ABCS for patients 134-0002 and 146-0002 at Week 24 were calculated after data-base lock)
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4.10.8.44 VABS-II Adaptive Behavior Composite Score by region (including patients where composite score was erroneously not calculated)

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Baseline	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	82.38 (11.326)	68.33 (13.382)
	Week 12	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	81.38 (10.070)	68.67 (11.483)
		Change from Baseline	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.70 (2.084)	-1.93 (2.447)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.63 (3.393)	
			95% CI for LS Mean Difference [2]	-4.70, 9.97	
			p-value MMRM [2]	0.4518	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.40	
			95% CI for SMD (Hedges' g)	-0.67, 1.47	
			p-value WRS[3]	0.8751	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

NOTE: Including patients where previously Adaptive Behavior Composite Score (ABCS) was erroneously not calculated (ABCS for patients 134-0002 and 146-0002 at Week 24 were calculated after data-base lock)

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VABS-II Adaptive Behavior Composite Score by region (including patients where composite score was erroneously not calculated)

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	78.88 (8.184)	65.67 (11.501)
		Change from Baseline	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-1.80 (1.670)	-4.93 (1.979)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.13 (2.808)	
			95% CI for LS Mean Difference [2]	-3.05, 9.31	
			p-value MMRM [2]	0.2885	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.58	
			95% CI for SMD (Hedges' g)	-0.50, 1.67	
			p-value WRS[3]	0.8775	
Non-US	Baseline	Absolute value	n (%)	12 (92.31)	5 (100.00)
			Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
			Mean (SD)	64.33 (28.279)	66.00 (18.507)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

NOTE: Including patients where previously Adaptive Behavior Composite Score (ABCS) was erroneously not calculated (ABCS for patients 134-0002 and 146-0002 at Week 24 were calculated after data-base lock)

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VABS-II Adaptive Behavior Composite Score by region (including patients where composite score was erroneously not calculated)

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	10 (76.92)	3 (60.00)
			Number of patients with missing data: n (%)	3 (23.08)	2 (40.00)
			Mean (SD)	72.20 (28.545)	82.00 (22.517)
		Change from Baseline	n (%)	10 (76.92)	3 (60.00)
			Number of patients with missing data: n (%)	3 (23.08)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	6.55 (5.771)	10.62 (8.976)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-4.07 (10.668)	
			95% CI for LS Mean Difference [2]	-26.81, 18.66	
			p-value MMRM [2]	0.7078	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.21	
			95% CI for SMD (Hedges' g)	-1.50, 1.08	
			p-value WRS[3]	0.1748	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Including patients where previously Adaptive Behavior Composite Score (ABCS) was erroneously not calculated (ABCS for patients 134-0002 and 146-0002 at Week 24 were calculated after data-base lock)
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VABS-II Adaptive Behavior Composite Score by region (including patients where composite score was erroneously not calculated)

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	11 (84.62)	5 (100.00)
			Number of patients with missing data: n (%)	2 (15.38)	0 (0.00)
			Mean (SD)	69.18 (25.059)	65.80 (10.208)
		Change from Baseline	n (%)	11 (84.62)	5 (100.00)
			Number of patients with missing data: n (%)	2 (15.38)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	4.22 (4.601)	-0.17 (6.814)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	4.39 (8.223)	
			95% CI for LS Mean Difference [2]	-13.36, 22.14	
			p-value MMRM [2]	0.6021	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.26	
			95% CI for SMD (Hedges' g)	-0.80, 1.32	
			p-value WRS[3]	1.0000	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Including patients where previously Adaptive Behavior Composite Score (ABCS) was erroneously not calculated (ABCS for patients 134-0002 and 146-0002 at Week 24 were calculated after data-base lock)
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4.10.8.45 VABS-II Adaptive Behavior Composite Score by GMFCS (including patients where composite score was erroneously not calculated)

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Baseline	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	84.38 (12.727)	70.40 (12.857)
	Week 12	Absolute value	n (%)	8 (88.89)	4 (80.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (20.00)
			Mean (SD)	84.38 (12.872)	79.00 (5.477)
		Change from Baseline	n (%)	8 (88.89)	4 (80.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	1.88 (3.325)	1.79 (4.560)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.08 (6.010)	
			95% CI for LS Mean Difference [2]	-13.31, 13.47	
			p-value MMRM [2]	0.9890	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.01	
			95% CI for SMD (Hedges' g)	-1.19, 1.21	
			p-value WRS[3]	0.6828	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

NOTE: Including patients where previously Adaptive Behavior Composite Score (ABCS) was erroneously not calculated (ABCS for patients 134-0002 and 146-0002 at Week 24 were calculated after data-base lock)

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VABS-II Adaptive Behavior Composite Score by GMFCS (including patients where composite score was erroneously not calculated)

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	82.50 (14.010)	71.60 (8.295)
		Change from Baseline	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.00 (3.584)	-2.81 (4.869)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.82 (6.411)	
			95% CI for LS Mean Difference [2]	-11.35, 16.99	
			p-value MMRM [2]	0.6691	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.24	
			95% CI for SMD (Hedges' g)	-0.88, 1.36	
			p-value WRS[3]	0.5113	
≥ II	Baseline	Absolute value	n (%)	12 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	63.00 (26.850)	64.67 (17.489)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Sensitivity analysis based on Wilcoxon rank sum test.

NOTE: Including patients where previously Adaptive Behavior Composite Score (ABCS) was erroneously not calculated (ABCS for patients 134-0002 and 146-0002 at Week 24 were calculated after data-base lock)

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VABS-II Adaptive Behavior Composite Score by GMFCS (including patients where composite score was erroneously not calculated)

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	10 (83.33)	5 (83.33)
			Number of patients with missing data: n (%)	2 (16.67)	1 (16.67)
			Mean (SD)	69.80 (26.486)	68.40 (20.550)
		Change from Baseline	n (%)	10 (83.33)	5 (83.33)
			Number of patients with missing data: n (%)	2 (16.67)	1 (16.67)
			LS Mean Change from Baseline (SE) [2]	5.98 (5.373)	2.97 (7.330)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.00 (9.089)	
			95% CI for LS Mean Difference [2]	-16.35, 22.36	
			p-value MMRM [2]	0.7456	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.16	
			95% CI for SMD (Hedges' g)	-0.91, 1.24	
			p-value WRS[3]	0.3556	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Including patients where previously Adaptive Behavior Composite Score (ABCS) was erroneously not calculated (ABCS for patients 134-0002 and 146-0002 at Week 24 were calculated after data-base lock)
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VABS-II Adaptive Behavior Composite Score by GMFCS (including patients where composite score was erroneously not calculated)

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	11 (91.67)	6 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	66.55 (21.519)	60.83 (9.867)
		Change from Baseline	n (%)	11 (91.67)	6 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	3.09 (3.703)	-3.57 (5.009)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	6.66 (6.231)	
			95% CI for LS Mean Difference [2]	-6.68, 20.01	
			p-value MMRM [2]	0.3028	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.50	
			95% CI for SMD (Hedges' g)	-0.51, 1.51	
			p-value WRS[3]	0.4510	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Sensitivity analysis based on Wilcoxon rank sum test.
NOTE: Including patients where previously Adaptive Behavior Composite Score (ABCS) was erroneously not calculated (ABCS for patients 134-0002 and 146-0002 at Week 24 were calculated after data-base lock)
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4.10.8.46 VABS-II Adaptive Behavior Composite Score responders ≥ 7,5 by gender (including patients where composite score was erroneously not calculated)

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Gender, p-value Chi-Square[1]	0.9760	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (14.29)
		Non-Responders [2]	10 (83.33)	7 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	3.57 (0.15, 85.68)	
		RR (95% CI)	3.08 (0.17, 56.25)	
		RD % (95% CI)	12.98 (-14.23, 40.19)	
		p-value – Fisher's Exact Test	0.5088	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	10 (83.33)	7 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	3.57 (0.15, 85.68)	
		RR (95% CI)	3.08 (0.17, 56.25)	
		RD % (95% CI)	12.98 (-14.23, 40.19)	
		p-value – Fisher's Exact Test	0.5088	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Including patients where previously Adaptive Behavior Composite Score (ABCS) was erroneously not calculated (ABCS for patients 134-0002 and 146-0002 at Week 24 were calculated after data-base lock)
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VABS-II Adaptive Behavior Composite Score responders ≥ 7,5 by gender (including patients where composite score was erroneously not calculated)

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (25.00)
		Non-Responders [2]	8 (88.89)	3 (75.00)
		Responders	1 (11.11)	1 (25.00)
		OR (95% CI)	0.38 (0.02, 8.10)	
		RR (95% CI)	0.44 (0.04, 5.46)	
		RD % (95% CI)	-13.89 (-61.03, 33.25)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	8 (88.89)	3 (75.00)
		Responders	1 (11.11)	1 (25.00)
		OR (95% CI)	0.38 (0.02, 8.10)	
		RR (95% CI)	0.44 (0.04, 5.46)	
		RD % (95% CI)	-13.89 (-61.03, 33.25)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Including patients where previously Adaptive Behavior Composite Score (ABCS) was erroneously not calculated (ABCS for patients 134-0002 and 146-0002 at Week 24 were calculated after data-base lock)
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4.10.8.47 VABS-II Adaptive Behavior Composite Score responders ≥ 7,5 by age group (including patients where composite score was erroneously not calculated)

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Age Group, p-value Chi-Square[1]	0.9774	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	10 (83.33)	4 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	2.14 (0.08, 54.22)	
		RR (95% CI)	1.92 (0.11, 33.44)	
		RD % (95% CI)	9.23 (-24.69, 43.15)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [2]	11 (91.67)	4 (100.00)
		Responders	1 (8.33)	0 (0.00)
		OR (95% CI)	1.17 (0.04, 34.52)	
		RR (95% CI)	1.15 (0.06, 23.88)	
		RD % (95% CI)	1.54 (-29.97, 33.05)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Including patients where previously Adaptive Behavior Composite Score (ABCS) was erroneously not calculated (ABCS for patients 134-0002 and 146-0002 at Week 24 were calculated after data-base lock)
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VABS-II Adaptive Behavior Composite Score responders ≥ 7,5 by age group (including patients where composite score was erroneously not calculated)

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	2 (28.57)
		Non-Responders [2]	8 (88.89)	6 (85.71)
		Responders	1 (11.11)	1 (14.29)
		OR (95% CI)	0.75 (0.04, 14.58)	
		RR (95% CI)	0.78 (0.06, 10.37)	
		RD % (95% CI)	-3.17 (-36.24, 29.89)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	7 (77.78)	6 (85.71)
		Responders	2 (22.22)	1 (14.29)
		OR (95% CI)	1.71 (0.12, 23.94)	
		RR (95% CI)	1.56 (0.17, 13.87)	
		RD % (95% CI)	7.94 (-29.61, 45.48)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Including patients where previously Adaptive Behavior Composite Score (ABCS) was erroneously not calculated (ABCS for patients 134-0002 and 146-0002 at Week 24 were calculated after data-base lock)
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4.10.8.48 VABS-II Adaptive Behavior Composite Score responders ≥ 7,5 by region (including patients where composite score was erroneously not calculated)

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*Region, p-value Chi-Square[1]	0.9996	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	7 (87.50)	6 (100.00)
		Responders	1 (12.50)	0 (0.00)
		OR (95% CI)	2.60 (0.09, 75.49)	
		RR (95% CI)	2.33 (0.11, 48.99)	
		RD % (95% CI)	9.52 (-21.41, 40.46)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [2]	8 (100.00)	6 (100.00)

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Including patients where previously Adaptive Behavior Composite Score (ABCS) was erroneously not calculated (ABCS for patients 134-0002 and 146-0002 at Week 24 were calculated after data-base lock)
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VABS-II Adaptive Behavior Composite Score responders ≥ 7,5 by region (including patients where composite score was erroneously not calculated)

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (23.08)	2 (40.00)
		Non-Responders [2]	11 (84.62)	4 (80.00)
		Responders	2 (15.38)	1 (20.00)
		OR (95% CI)	0.73 (0.05, 10.39)	
		RR (95% CI)	0.77 (0.09, 6.72)	
		RD % (95% CI)	-4.62 (-44.79, 35.56)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (15.38)	0 (0.00)
		Non-Responders [2]	10 (76.92)	4 (80.00)
		Responders	3 (23.08)	1 (20.00)
		OR (95% CI)	1.20 (0.09, 15.26)	
		RR (95% CI)	1.15 (0.15, 8.65)	
		RD % (95% CI)	3.08 (-38.80, 44.96)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Including patients where previously Adaptive Behavior Composite Score (ABCS) was erroneously not calculated (ABCS for patients 134-0002 and 146-0002 at Week 24 were calculated after data-base lock)
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4.10.8.49 VABS-II Adaptive Behavior Composite Score responders ≥ 7,5 by GMFCS (including patients where composite score was erroneously not calculated)

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test at Week 24	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.9668	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (20.00)
		Non-Responders [2]	8 (88.89)	4 (80.00)
		Responders	1 (11.11)	1 (20.00)
		OR (95% CI)	0.50 (0.02, 10.25)	
		RR (95% CI)	0.56 (0.04, 7.09)	
		RD % (95% CI)	-8.89 (-49.52, 31.74)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [2]	8 (88.89)	4 (80.00)
		Responders	1 (11.11)	1 (20.00)
		OR (95% CI)	0.50 (0.02, 10.25)	
		RR (95% CI)	0.56 (0.04, 7.09)	
		RD % (95% CI)	-8.89 (-49.52, 31.74)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Including patients where previously Adaptive Behavior Composite Score (ABCS) was erroneously not calculated (ABCS for patients 134-0002 and 146-0002 at Week 24 were calculated after data-base lock)
Program: t-qs-categ-sub.sas
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VABS-II Adaptive Behavior Composite Score responders ≥ 7,5 by GMFCS (including patients where composite score was erroneously not calculated)

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (16.67)
		Non-Responders [2]	10 (83.33)	6 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	3.10 (0.13, 75.18)	
		RR (95% CI)	2.69 (0.15, 48.64)	
		RD % (95% CI)	12.09 (-16.60, 40.78)	
		p-value – Fisher's Exact Test	0.5294	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [2]	10 (83.33)	6 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	3.10 (0.13, 75.18)	
		RR (95% CI)	2.69 (0.15, 48.64)	
		RD % (95% CI)	12.09 (-16.60, 40.78)	
		p-value – Fisher's Exact Test	0.5294	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Including patients where previously Adaptive Behavior Composite Score (ABCS) was erroneously not calculated (ABCS for patients 134-0002 and 146-0002 at Week 24 were calculated after data-base lock)
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4.10.9 Subgruppenanalysen für den Endpunkt CaGI-C

4.10.9.1 CaGI-C ability to walk by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.0705	
Male	Week 12	Absolute value	n (%)	10 (83.33)	6 (85.71)
			Number of patients with missing data: n (%)	2 (16.67)	1 (14.29)
			Mean (SD)	2.60 (0.516)	2.67 (0.516)
			LS Mean (SE) [2]	2.58 (0.163)	2.72 (0.210)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.14 (0.266)	
			95% CI for LS Mean Difference [2]	-0.71, 0.43	
			p-value MMRM [2]	0.6074	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.25	
			95% CI for SMD (Hedges' g)	-1.26, 0.77	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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1.4.9 CaGI-C
CaGI-C ability to walk by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	10 (83.33)	7 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	2.50 (0.850)	3.00 (0.577)
			LS Mean (SE) [2]	2.46 (0.237)	3.00 (0.285)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.54 (0.371)	
			95% CI for LS Mean Difference [2]	-1.33, 0.25	
			p-value MMRM [2]	0.1645	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.66	
			95% CI for SMD (Hedges' g)	-1.66, 0.33	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.
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1.4.9 CaGI-C
CaGI-C ability to walk by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	3.00 (0.000)	2.50 (1.000)
			LS Mean (SE) [2]	3.02 (0.212)	2.50 (0.283)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.52 (0.354)	
			95% CI for LS Mean Difference [2]	-0.27, 1.31	
			p-value MMRM [2]	0.1703	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.82	
			95% CI for SMD (Hedges' g)	-0.47, 2.10	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.
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1.4.9 CaGI-C
CaGI-C ability to walk by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	2.78 (0.441)	2.00 (1.155)
			LS Mean (SE) [2]	2.78 (0.237)	2.00 (0.355)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.78 (0.427)	
			95% CI for LS Mean Difference [2]	-0.16, 1.72	
			p-value MMRM [2]	0.0959	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.97	
			95% CI for SMD (Hedges' g)	-0.27, 2.22	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.
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4.10.9.2 CaGI-C ability to walk by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.0719	
<10.5 years old at screening	Week 12	Absolute value	n (%)	9 (75.00)	3 (75.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
			Mean (SD)	2.67 (0.500)	3.00 (0.000)
			LS Mean (SE) [2]	2.68 (0.151)	3.17 (0.260)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.49 (0.301)	
			95% CI for LS Mean Difference [2]	-1.16, 0.18	
			p-value MMRM [2]	0.1329	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.96	
			95% CI for SMD (Hedges' g)	-2.33, 0.42	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-C ability to walk by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	2.36 (0.674)	2.50 (1.291)
			LS Mean (SE) [2]	2.36 (0.258)	2.50 (0.428)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.14 (0.500)	
			95% CI for LS Mean Difference [2]	-1.22, 0.94	
			p-value MMRM [2]	0.7895	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.14	
			95% CI for SMD (Hedges' g)	-1.29, 1.00	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-C ability to walk by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	8 (88.89)	7 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.88 (0.354)	2.43 (0.787)
			LS Mean (SE) [2]	2.88 (0.203)	2.43 (0.221)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.45 (0.300)	
			95% CI for LS Mean Difference [2]	-0.19, 1.10	
			p-value MMRM [2]	0.1545	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.71	
			95% CI for SMD (Hedges' g)	-0.34, 1.76	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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CaGI-C ability to walk by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	8 (88.89)	7 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	3.00 (0.535)	2.71 (0.756)
			LS Mean (SE) [2]	2.92 (0.230)	2.71 (0.251)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.21 (0.340)	
			95% CI for LS Mean Difference [2]	-0.53, 0.94	
			p-value MMRM [2]	0.5568	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.28	
			95% CI for SMD (Hedges' g)	-0.74, 1.30	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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4.10.9.3 CaGI-C ability to walk by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.8314	
US	Week 12	Absolute value	n (%)	7 (87.50)	5 (83.33)
			Number of patients with missing data: n (%)	1 (12.50)	1 (16.67)
			Mean (SD)	2.86 (0.378)	2.60 (0.894)
			LS Mean (SE) [2]	2.88 (0.236)	2.74 (0.276)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.14 (0.363)	
			95% CI for LS Mean Difference [2]	-0.66, 0.93	
			p-value MMRM [2]	0.7146	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.20	
			95% CI for SMD (Hedges' g)	-0.96, 1.35	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C ability to walk by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	2.75 (0.886)	2.67 (1.033)
			LS Mean (SE) [2]	2.75 (0.336)	2.67 (0.388)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.08 (0.513)	
			95% CI for LS Mean Difference [2]	-1.03, 1.20	
			p-value MMRM [2]	0.8737	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.08	
			95% CI for SMD (Hedges' g)	-0.98, 1.14	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C ability to walk by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	10 (76.92)	5 (100.00)
			Number of patients with missing data: n (%)	3 (23.08)	0 (0.00)
			Mean (SD)	2.70 (0.483)	2.60 (0.548)
			LS Mean (SE) [2]	2.70 (0.161)	2.60 (0.225)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.10 (0.277)	
			95% CI for LS Mean Difference [2]	-0.50, 0.70	
			p-value MMRM [2]	0.7253	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.18	
			95% CI for SMD (Hedges' g)	-0.90, 1.25	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C ability to walk by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	11 (84.62)	5 (100.00)
			Number of patients with missing data: n (%)	2 (15.38)	0 (0.00)
			Mean (SD)	2.55 (0.522)	2.60 (0.894)
			LS Mean (SE) [2]	2.54 (0.198)	2.60 (0.291)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.06 (0.352)	
			95% CI for LS Mean Difference [2]	-0.82, 0.69	
			p-value MMRM [2]	0.8640	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.09	
			95% CI for SMD (Hedges' g)	-1.14, 0.97	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.9.4 CaGI-C ability to walk by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.7539	
I	Week 12	Absolute value	n (%)	8 (88.89)	4 (80.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (20.00)
			Mean (SD)	2.88 (0.354)	2.50 (1.000)
			LS Mean (SE) [2]	2.87 (0.226)	2.66 (0.302)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.22 (0.377)	
			95% CI for LS Mean Difference [2]	-0.61, 1.05	
			p-value MMRM [2]	0.5741	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.31	
			95% CI for SMD (Hedges' g)	-0.90, 1.51	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C ability to walk by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.63 (0.916)	2.80 (1.095)
			LS Mean (SE) [2]	2.62 (0.348)	2.80 (0.441)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.18 (0.562)	
			95% CI for LS Mean Difference [2]	-1.41, 1.06	
			p-value MMRM [2]	0.7612	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.16	
			95% CI for SMD (Hedges' g)	-1.28, 0.96	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C ability to walk by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	9 (75.00)	6 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			Mean (SD)	2.67 (0.500)	2.67 (0.516)
			LS Mean (SE) [2]	2.67 (0.172)	2.67 (0.207)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.00 (0.269)	
			95% CI for LS Mean Difference [2]	-0.58, 0.58	
			p-value MMRM [2]	0.9984	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.00	
			95% CI for SMD (Hedges' g)	-1.03, 1.03	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C ability to walk by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	11 (91.67)	6 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	2.64 (0.505)	2.50 (0.837)
			LS Mean (SE) [2]	2.63 (0.193)	2.50 (0.259)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.13 (0.323)	
			95% CI for LS Mean Difference [2]	-0.56, 0.82	
			p-value MMRM [2]	0.6891	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.19	
			95% CI for SMD (Hedges' g)	-0.81, 1.19	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.9.5 CaGI-C ability to walk responders - any improvement by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Gender, p-value Chi-Square[1]	0.1272	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (14.29)
		Non-Responders [1]	8 (66.67)	5 (71.43)
		Responders	4 (33.33)	2 (28.57)
		OR (95% CI)	1.25 (0.16, 9.54)	
		RR (95% CI)	1.17 (0.28, 4.82)	
		RD % (95% CI)	4.76 (-38.03, 47.56)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [1]	7 (58.33)	6 (85.71)
		Responders	5 (41.67)	1 (14.29)
		OR (95% CI)	4.29 (0.39, 47.62)	
		RR (95% CI)	2.92 (0.42, 20.18)	
		RD % (95% CI)	27.38 (-10.70, 65.46)	
		p-value – Fisher's Exact Test	0.3331	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CaGI-C ability to walk responders - any improvement by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (22.22)	0 (0.00)
		Non-Responders [1]	9 (100.00)	3 (75.00)
		Responders	0 (0.00)	1 (25.00)
		OR (95% CI)	0.12 (0.00, 3.78)	
		RR (95% CI)	0.17 (0.01, 3.40)	
		RD % (95% CI)	-25.00 (-67.38, 17.38)	
		p-value – Fisher's Exact Test	0.3077	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	7 (77.78)	2 (50.00)
		Responders	2 (22.22)	2 (50.00)
		OR (95% CI)	0.29 (0.02, 3.52)	
		RR (95% CI)	0.44 (0.09, 2.13)	
		RD % (95% CI)	-27.78 (-83.80, 28.25)	
		p-value – Fisher's Exact Test	0.5301	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.9.6 CaGI-C ability to walk responders - any improvement by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Age Group, p-value Chi-Square[1]	0.8799	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (25.00)	1 (25.00)
		Non-Responders [1]	9 (75.00)	4 (100.00)
		Responders	3 (25.00)	0 (0.00)
		OR (95% CI)	3.32 (0.14, 78.81)	
		RR (95% CI)	2.69 (0.17, 43.31)	
		RD % (95% CI)	16.92 (-18.75, 52.60)	
		p-value – Fisher's Exact Test	0.5286	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [1]	6 (50.00)	2 (50.00)
		Responders	6 (50.00)	2 (50.00)
		OR (95% CI)	1.00 (0.10, 9.61)	
		RR (95% CI)	1.00 (0.32, 3.10)	
		RD % (95% CI)	0.00 (-56.58, 56.58)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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CaGI-C ability to walk responders - any improvement by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	8 (88.89)	4 (57.14)
		Responders	1 (11.11)	3 (42.86)
		OR (95% CI)	0.17 (0.01, 2.16)	
		RR (95% CI)	0.26 (0.03, 1.99)	
		RD % (95% CI)	-31.75 (-73.76, 10.27)	
		p-value – Fisher's Exact Test	0.2615	
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	8 (88.89)	6 (85.71)
		Responders	1 (11.11)	1 (14.29)
		OR (95% CI)	0.75 (0.04, 14.58)	
		RR (95% CI)	0.78 (0.06, 10.37)	
		RD % (95% CI)	-3.17 (-36.24, 29.89)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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4.10.9.7 CaGI-C ability to walk responders - any improvement by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Region, p-value Chi-Square[1]	0.4448	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (12.50)	1 (16.67)
		Non-Responders [1]	7 (87.50)	5 (83.33)
		Responders	1 (12.50)	1 (16.67)
		OR (95% CI)	0.71 (0.04, 14.35)	
		RR (95% CI)	0.75 (0.06, 9.72)	
		RD % (95% CI)	-4.17 (-41.78, 33.44)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	6 (75.00)	4 (66.67)
		Responders	2 (25.00)	2 (33.33)
		OR (95% CI)	0.67 (0.06, 6.87)	
		RR (95% CI)	0.75 (0.14, 3.90)	
		RD % (95% CI)	-8.33 (-56.53, 39.87)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CaGI-C ability to walk responders - any improvement by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (23.08)	0 (0.00)
		Non-Responders [1]	10 (76.92)	3 (60.00)
		Responders	3 (23.08)	2 (40.00)
		OR (95% CI)	0.45 (0.05, 4.09)	
		RR (95% CI)	0.58 (0.13, 2.49)	
		RD % (95% CI)	-16.92 (-65.59, 31.74)	
		p-value – Fisher's Exact Test	0.5827	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (15.38)	0 (0.00)
		Non-Responders [1]	8 (61.54)	4 (80.00)
		Responders	5 (38.46)	1 (20.00)
		OR (95% CI)	2.50 (0.21, 29.25)	
		RR (95% CI)	1.92 (0.29, 12.64)	
		RD % (95% CI)	18.46 (-25.46, 62.38)	
		p-value – Fisher's Exact Test	0.6148	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.9.8 CaGI-C ability to walk responders - any improvement by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.6827	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (20.00)
		Non-Responders [1]	8 (88.89)	4 (80.00)
		Responders	1 (11.11)	1 (20.00)
		OR (95% CI)	0.50 (0.02, 10.25)	
		RR (95% CI)	0.56 (0.04, 7.09)	
		RD % (95% CI)	-8.89 (-49.52, 31.74)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	6 (66.67)	4 (80.00)
		Responders	3 (33.33)	1 (20.00)
		OR (95% CI)	2.00 (0.15, 26.73)	
		RR (95% CI)	1.67 (0.23, 12.09)	
		RD % (95% CI)	13.33 (-33.33, 60.00)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CaGI-C ability to walk responders - any improvement by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (25.00)	0 (0.00)
		Non-Responders [1]	9 (75.00)	4 (66.67)
		Responders	3 (25.00)	2 (33.33)
		OR (95% CI)	0.67 (0.08, 5.68)	
		RR (95% CI)	0.75 (0.17, 3.35)	
		RD % (95% CI)	-8.33 (-53.31, 36.64)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [1]	8 (66.67)	4 (66.67)
		Responders	4 (33.33)	2 (33.33)
		OR (95% CI)	1.00 (0.13, 8.00)	
		RR (95% CI)	1.00 (0.25, 4.00)	
		RD % (95% CI)	0.00 (-46.20, 46.20)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.9.9 CaGI-C dependance on assistive device by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.1359	
Male	Week 12	Absolute value	n (%)	8 (66.67)	5 (71.43)
			Number of patients with missing data: n (%)	4 (33.33)	2 (28.57)
			Mean (SD)	2.75 (0.463)	2.60 (0.894)
			LS Mean (SE) [2]	2.74 (0.233)	2.58 (0.296)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.16 (0.377)	
			95% CI for LS Mean Difference [2]	-0.67, 0.99	
			p-value MMRM [2]	0.6798	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.22	
			95% CI for SMD (Hedges' g)	-0.91, 1.34	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C dependance on assistive device by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	9 (75.00)	6 (85.71)
			Number of patients with missing data: n (%)	3 (25.00)	1 (14.29)
			Mean (SD)	2.44 (0.726)	2.67 (0.516)
			LS Mean (SE) [2]	2.44 (0.218)	2.67 (0.267)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.22 (0.345)	
			95% CI for LS Mean Difference [2]	-0.97, 0.52	
			p-value MMRM [2]	0.5302	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.31	
			95% CI for SMD (Hedges' g)	-1.35, 0.73	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C dependance on assistive device by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	3.00 (0.000)	2.50 (0.577)
			LS Mean (SE) [2]	3.01 (0.106)	2.50 (0.154)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.51 (0.187)	
			95% CI for LS Mean Difference [2]	0.10, 0.92	
			p-value MMRM [2]	0.0190 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.58	
			95% CI for SMD (Hedges' g)	0.15, 3.01	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C dependance on assistive device by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	2.89 (0.333)	2.00 (1.155)
			LS Mean (SE) [2]	2.89 (0.222)	2.00 (0.333)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.89 (0.401)	
			95% CI for LS Mean Difference [2]	0.01, 1.77	
			p-value MMRM [2]	0.0485 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.19	
			95% CI for SMD (Hedges' g)	-0.09, 2.47	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.
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4.10.9.10 CaGI-C dependance on assistive device by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.9602	
<10.5 years old at screening	Week 12	Absolute value	n (%)	8 (66.67)	3 (75.00)
			Number of patients with missing data: n (%)	4 (33.33)	1 (25.00)
			Mean (SD)	2.88 (0.354)	2.67 (0.577)
			LS Mean (SE) [2]	2.88 (0.142)	2.67 (0.232)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.21 (0.272)	
			95% CI for LS Mean Difference [2]	-0.40, 0.81	
			p-value MMRM [2]	0.4606	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.46	
			95% CI for SMD (Hedges' g)	-0.89, 1.80	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-C dependance on assistive device by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	2.50 (0.707)	2.00 (0.816)
			LS Mean (SE) [2]	2.50 (0.233)	2.00 (0.368)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.50 (0.435)	
			95% CI for LS Mean Difference [2]	-0.45, 1.45	
			p-value MMRM [2]	0.2732	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.61	
			95% CI for SMD (Hedges' g)	-0.57, 1.80	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-C dependance on assistive device by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	7 (77.78)	6 (85.71)
			Number of patients with missing data: n (%)	2 (22.22)	1 (14.29)
			Mean (SD)	2.86 (0.378)	2.50 (0.837)
			LS Mean (SE) [2]	2.87 (0.236)	2.50 (0.255)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.37 (0.347)	
			95% CI for LS Mean Difference [2]	-0.40, 1.13	
			p-value MMRM [2]	0.3146	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.52	
			95% CI for SMD (Hedges' g)	-0.59, 1.64	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-C dependance on assistive device by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	8 (88.89)	6 (85.71)
			Number of patients with missing data: n (%)	1 (11.11)	1 (14.29)
			Mean (SD)	2.88 (0.354)	2.67 (0.816)
			LS Mean (SE) [2]	2.88 (0.209)	2.67 (0.242)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.21 (0.320)	
			95% CI for LS Mean Difference [2]	-0.49, 0.91	
			p-value MMRM [2]	0.5271	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.32	
			95% CI for SMD (Hedges' g)	-0.75, 1.38	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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4.10.9.11 CaGI-C dependance on assistive device by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.4946	
US	Week 12	Absolute value	n (%)	7 (87.50)	5 (83.33)
			Number of patients with missing data: n (%)	1 (12.50)	1 (16.67)
			Mean (SD)	2.86 (0.378)	2.40 (0.894)
			LS Mean (SE) [2]	2.86 (0.243)	2.39 (0.288)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.47 (0.377)	
			95% CI for LS Mean Difference [2]	-0.37, 1.31	
			p-value MMRM [2]	0.2398	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.64	
			95% CI for SMD (Hedges' g)	-0.54, 1.83	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C dependance on assistive device by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	2.63 (0.744)	2.33 (0.816)
			LS Mean (SE) [2]	2.63 (0.274)	2.33 (0.316)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.29 (0.419)	
			95% CI for LS Mean Difference [2]	-0.62, 1.20	
			p-value MMRM [2]	0.4992	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.34	
			95% CI for SMD (Hedges' g)	-0.73, 1.41	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C dependance on assistive device by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	8 (61.54)	4 (80.00)
			Number of patients with missing data: n (%)	5 (38.46)	1 (20.00)
			Mean (SD)	2.88 (0.354)	2.75 (0.500)
			LS Mean (SE) [2]	2.85 (0.131)	2.75 (0.198)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.10 (0.237)	
			95% CI for LS Mean Difference [2]	-0.42, 0.62	
			p-value MMRM [2]	0.6809	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.24	
			95% CI for SMD (Hedges' g)	-0.97, 1.44	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C dependance on assistive device by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	10 (76.92)	4 (80.00)
			Number of patients with missing data: n (%)	3 (23.08)	1 (20.00)
			Mean (SD)	2.70 (0.483)	2.50 (1.000)
			LS Mean (SE) [2]	2.70 (0.206)	2.50 (0.326)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.20 (0.386)	
			95% CI for LS Mean Difference [2]	-0.64, 1.04	
			p-value MMRM [2]	0.6135	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.28	
			95% CI for SMD (Hedges' g)	-0.89, 1.44	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.9.12 CaGI-C dependance on assistive device by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.9018	
I	Week 12	Absolute value	n (%)	8 (88.89)	4 (80.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (20.00)
			Mean (SD)	3.00 (0.000)	2.75 (0.500)
			LS Mean (SE) [2]	3.00 (0.095)	2.73 (0.131)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.27 (0.162)	
			95% CI for LS Mean Difference [2]	-0.08, 0.63	
			p-value MMRM [2]	0.1209	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.90	
			95% CI for SMD (Hedges' g)	-0.36, 2.17	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C dependance on assistive device by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.63 (0.744)	2.40 (0.894)
			LS Mean (SE) [2]	2.62 (0.284)	2.40 (0.359)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.22 (0.457)	
			95% CI for LS Mean Difference [2]	-0.78, 1.23	
			p-value MMRM [2]	0.6323	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.25	
			95% CI for SMD (Hedges' g)	-0.87, 1.37	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C dependance on assistive device by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	7 (58.33)	5 (83.33)
			Number of patients with missing data: n (%)	5 (41.67)	1 (16.67)
			Mean (SD)	2.71 (0.488)	2.40 (0.894)
			LS Mean (SE) [2]	2.71 (0.257)	2.40 (0.302)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.31 (0.397)	
			95% CI for LS Mean Difference [2]	-0.57, 1.19	
			p-value MMRM [2]	0.4528	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.40	
			95% CI for SMD (Hedges' g)	-0.76, 1.56	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C dependance on assistive device by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	10 (83.33)	5 (83.33)
			Number of patients with missing data: n (%)	2 (16.67)	1 (16.67)
			Mean (SD)	2.70 (0.483)	2.40 (0.894)
			LS Mean (SE) [2]	2.70 (0.202)	2.40 (0.286)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.30 (0.350)	
			95% CI for LS Mean Difference [2]	-0.46, 1.06	
			p-value MMRM [2]	0.4065	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.43	
			95% CI for SMD (Hedges' g)	-0.66, 1.51	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.9.13 CaGI-C dependance on assistive device responders - any improvement by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Gender, p-value Chi-Square[1]	0.1981	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	4 (33.33)	2 (28.57)
		Non-Responders [1]	10 (83.33)	6 (85.71)
		Responders	2 (16.67)	1 (14.29)
		OR (95% CI)	1.20 (0.09, 16.24)	
		RR (95% CI)	1.17 (0.13, 10.66)	
		RD % (95% CI)	2.38 (-31.03, 35.80)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (25.00)	1 (14.29)
		Non-Responders [1]	8 (66.67)	5 (71.43)
		Responders	4 (33.33)	2 (28.57)
		OR (95% CI)	1.25 (0.16, 9.54)	
		RR (95% CI)	1.17 (0.28, 4.82)	
		RD % (95% CI)	4.76 (-38.03, 47.56)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CaGI-C dependance on assistive device responders - any improvement by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (22.22)	0 (0.00)
		Non-Responders [1]	9 (100.00)	2 (50.00)
		Responders	0 (0.00)	2 (50.00)
		OR (95% CI)	0.05 (0.00, 1.49)	
		RR (95% CI)	0.10 (0.01, 1.71)	
		RD % (95% CI)	-45.00 (-90.86, 0.86)	
		p-value – Fisher's Exact Test	0.0769	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	8 (88.89)	2 (50.00)
		Responders	1 (11.11)	2 (50.00)
		OR (95% CI)	0.13 (0.01, 2.18)	
		RR (95% CI)	0.22 (0.03, 1.80)	
		RD % (95% CI)	-38.89 (-92.02, 14.24)	
		p-value – Fisher's Exact Test	0.2028	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.9.14 CaGI-C dependance on assistive device responders - any improvement by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Age Group, p-value Chi-Square[1]	0.4519	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	4 (33.33)	1 (25.00)
		Non-Responders [1]	11 (91.67)	3 (75.00)
		Responders	1 (8.33)	1 (25.00)
		OR (95% CI)	0.27 (0.01, 5.77)	
		RR (95% CI)	0.33 (0.03, 4.19)	
		RD % (95% CI)	-16.67 (-61.89, 28.56)	
		p-value – Fisher's Exact Test	0.4500	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [1]	8 (66.67)	1 (25.00)
		Responders	4 (33.33)	3 (75.00)
		OR (95% CI)	0.17 (0.01, 2.16)	
		RR (95% CI)	0.44 (0.17, 1.18)	
		RD % (95% CI)	-41.67 (-91.79, 8.45)	
		p-value – Fisher's Exact Test	0.2615	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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CaGI-C dependance on assistive device responders - any improvement by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (22.22)	1 (14.29)
		Non-Responders [1]	8 (88.89)	5 (71.43)
		Responders	1 (11.11)	2 (28.57)
		OR (95% CI)	0.31 (0.02, 4.41)	
		RR (95% CI)	0.39 (0.04, 3.47)	
		RD % (95% CI)	-17.46 (-56.72, 21.80)	
		p-value – Fisher's Exact Test	0.5500	
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (14.29)
		Non-Responders [1]	8 (88.89)	6 (85.71)
		Responders	1 (11.11)	1 (14.29)
		OR (95% CI)	0.75 (0.04, 14.58)	
		RR (95% CI)	0.78 (0.06, 10.37)	
		RD % (95% CI)	-3.17 (-36.24, 29.89)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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4.10.9.15 CaGI-C dependance on assistive device responders - any improvement by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Region, p-value Chi-Square[1]	0.4608	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (12.50)	1 (16.67)
		Non-Responders [1]	7 (87.50)	4 (66.67)
		Responders	1 (12.50)	2 (33.33)
		OR (95% CI)	0.29 (0.02, 4.24)	
		RR (95% CI)	0.38 (0.04, 3.23)	
		RD % (95% CI)	-20.83 (-64.97, 23.30)	
		p-value – Fisher's Exact Test	0.5385	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	6 (75.00)	3 (50.00)
		Responders	2 (25.00)	3 (50.00)
		OR (95% CI)	0.33 (0.03, 3.20)	
		RR (95% CI)	0.50 (0.12, 2.12)	
		RD % (95% CI)	-25.00 (-75.01, 25.01)	
		p-value – Fisher's Exact Test	0.5804	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CaGI-C dependance on assistive device responders - any improvement by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	5 (38.46)	1 (20.00)
		Non-Responders [1]	12 (92.31)	4 (80.00)
		Responders	1 (7.69)	1 (20.00)
		OR (95% CI)	0.33 (0.02, 6.65)	
		RR (95% CI)	0.38 (0.03, 5.04)	
		RD % (95% CI)	-12.31 (-50.24, 25.63)	
		p-value – Fisher's Exact Test	0.4902	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (23.08)	1 (20.00)
		Non-Responders [1]	10 (76.92)	4 (80.00)
		Responders	3 (23.08)	1 (20.00)
		OR (95% CI)	1.20 (0.09, 15.26)	
		RR (95% CI)	1.15 (0.15, 8.65)	
		RD % (95% CI)	3.08 (-38.80, 44.96)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.9.16 CaGI-C dependance on assistive device responders - any improvement by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.7868	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (20.00)
		Non-Responders [1]	9 (100.00)	4 (80.00)
		Responders	0 (0.00)	1 (20.00)
		OR (95% CI)	0.16 (0.01, 4.69)	
		RR (95% CI)	0.20 (0.01, 4.17)	
		RD % (95% CI)	-20.00 (-57.19, 17.19)	
		p-value – Fisher's Exact Test	0.3571	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	7 (77.78)	3 (60.00)
		Responders	2 (22.22)	2 (40.00)
		OR (95% CI)	0.43 (0.04, 4.64)	
		RR (95% CI)	0.56 (0.11, 2.83)	
		RD % (95% CI)	-17.78 (-68.59, 33.03)	
		p-value – Fisher's Exact Test	0.5804	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CaGI-C dependance on assistive device responders - any improvement by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	5 (41.67)	1 (16.67)
		Non-Responders [1]	10 (83.33)	4 (66.67)
		Responders	2 (16.67)	2 (33.33)
		OR (95% CI)	0.40 (0.04, 3.90)	
		RR (95% CI)	0.50 (0.09, 2.73)	
		RD % (95% CI)	-16.67 (-59.88, 26.55)	
		p-value – Fisher's Exact Test	0.5686	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (16.67)
		Non-Responders [1]	9 (75.00)	4 (66.67)
		Responders	3 (25.00)	2 (33.33)
		OR (95% CI)	0.67 (0.08, 5.68)	
		RR (95% CI)	0.75 (0.17, 3.35)	
		RD % (95% CI)	-8.33 (-53.31, 36.64)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.9.17 CaGI-C fine motor skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.9624	
Male	Week 12	Absolute value	n (%)	10 (83.33)	6 (85.71)
			Number of patients with missing data: n (%)	2 (16.67)	1 (14.29)
			Mean (SD)	2.70 (0.483)	2.50 (0.548)
			LS Mean (SE) [2]	2.69 (0.161)	2.53 (0.208)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.16 (0.263)	
			95% CI for LS Mean Difference [2]	-0.40, 0.73	
			p-value MMRM [2]	0.5452	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.29	
			95% CI for SMD (Hedges' g)	-0.72, 1.31	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C fine motor skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	10 (83.33)	7 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	2.40 (0.516)	2.43 (0.535)
			LS Mean (SE) [2]	2.38 (0.167)	2.43 (0.199)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.05 (0.259)	
			95% CI for LS Mean Difference [2]	-0.60, 0.50	
			p-value MMRM [2]	0.8520	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.09	
			95% CI for SMD (Hedges' g)	-1.05, 0.88	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C fine motor skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	2.86 (0.378)	3.00 (0.000)
			LS Mean (SE) [2]	2.84 (0.115)	3.00 (0.154)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.16 (0.192)	
			95% CI for LS Mean Difference [2]	-0.59, 0.27	
			p-value MMRM [2]	0.4214	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.46	
			95% CI for SMD (Hedges' g)	-1.71, 0.79	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C fine motor skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	2.78 (0.441)	2.25 (0.957)
			LS Mean (SE) [2]	2.78 (0.209)	2.25 (0.313)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.53 (0.376)	
			95% CI for LS Mean Difference [2]	-0.30, 1.36	
			p-value MMRM [2]	0.1880	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.75	
			95% CI for SMD (Hedges' g)	-0.47, 1.97	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.9.18 CaGI-C fine motor skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.2834	
<10.5 years old at screening	Week 12	Absolute value	n (%)	9 (75.00)	3 (75.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
			Mean (SD)	2.78 (0.441)	2.33 (0.577)
			LS Mean (SE) [2]	2.78 (0.160)	2.34 (0.279)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.44 (0.321)	
			95% CI for LS Mean Difference [2]	-0.28, 1.15	
			p-value MMRM [2]	0.2033	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.80	
			95% CI for SMD (Hedges' g)	-0.55, 2.15	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-C fine motor skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	2.55 (0.522)	2.25 (0.957)
			LS Mean (SE) [2]	2.55 (0.196)	2.25 (0.325)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.30 (0.379)	
			95% CI for LS Mean Difference [2]	-0.52, 1.11	
			p-value MMRM [2]	0.4496	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.41	
			95% CI for SMD (Hedges' g)	-0.74, 1.57	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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CaGI-C fine motor skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	8 (88.89)	7 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.75 (0.463)	2.86 (0.378)
			LS Mean (SE) [2]	2.72 (0.149)	2.86 (0.161)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.14 (0.220)	
			95% CI for LS Mean Difference [2]	-0.61, 0.34	
			p-value MMRM [2]	0.5409	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.30	
			95% CI for SMD (Hedges' g)	-1.32, 0.73	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-C fine motor skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	8 (88.89)	7 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.63 (0.518)	2.43 (0.535)
			LS Mean (SE) [2]	2.56 (0.189)	2.43 (0.204)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.13 (0.278)	
			95% CI for LS Mean Difference [2]	-0.47, 0.74	
			p-value MMRM [2]	0.6402	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.22	
			95% CI for SMD (Hedges' g)	-0.79, 1.24	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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4.10.9.19 CaGI-C fine motor skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.3384	
US	Week 12	Absolute value	n (%)	7 (87.50)	5 (83.33)
			Number of patients with missing data: n (%)	1 (12.50)	1 (16.67)
			Mean (SD)	2.71 (0.488)	2.40 (0.548)
			LS Mean (SE) [2]	2.74 (0.192)	2.45 (0.227)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.29 (0.297)	
			95% CI for LS Mean Difference [2]	-0.36, 0.95	
			p-value MMRM [2]	0.3461	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.51	
			95% CI for SMD (Hedges' g)	-0.66, 1.68	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C fine motor skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	2.63 (0.518)	2.50 (0.548)
			LS Mean (SE) [2]	2.63 (0.187)	2.50 (0.217)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.12 (0.286)	
			95% CI for LS Mean Difference [2]	-0.50, 0.75	
			p-value MMRM [2]	0.6703	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.21	
			95% CI for SMD (Hedges' g)	-0.85, 1.27	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C fine motor skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	10 (76.92)	5 (100.00)
			Number of patients with missing data: n (%)	3 (23.08)	0 (0.00)
			Mean (SD)	2.80 (0.422)	3.00 (0.000)
			LS Mean (SE) [2]	2.78 (0.110)	3.00 (0.156)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.22 (0.191)	
			95% CI for LS Mean Difference [2]	-0.63, 0.19	
			p-value MMRM [2]	0.2655	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.58	
			95% CI for SMD (Hedges' g)	-1.68, 0.52	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C fine motor skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	11 (84.62)	5 (100.00)
			Number of patients with missing data: n (%)	2 (15.38)	0 (0.00)
			Mean (SD)	2.55 (0.522)	2.20 (0.837)
			LS Mean (SE) [2]	2.49 (0.195)	2.20 (0.289)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.29 (0.349)	
			95% CI for LS Mean Difference [2]	-0.47, 1.05	
			p-value MMRM [2]	0.4207	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.41	
			95% CI for SMD (Hedges' g)	-0.66, 1.47	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.9.20 CaGI-C fine motor skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.4176	
I	Week 12	Absolute value	n (%)	8 (88.89)	4 (80.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (20.00)
			Mean (SD)	3.00 (0.000)	3.00 (0.000)
			LS Mean (SE) [2]	3.00 (0.117)	3.00 (0.169)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.00 (0.205)	
			95% CI for LS Mean Difference [2]	-0.43, 0.43	
			p-value MMRM [2]	1.0000	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.00	
			95% CI for SMD (Hedges' g)	-1.20, 1.20	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C fine motor skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.75 (0.463)	2.80 (0.447)
			LS Mean (SE) [2]	2.75 (0.117)	2.80 (0.148)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.05 (0.189)	
			95% CI for LS Mean Difference [2]	-0.44, 0.34	
			p-value MMRM [2]	0.7936	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.14	
			95% CI for SMD (Hedges' g)	-1.26, 0.98	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C fine motor skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	9 (75.00)	6 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			Mean (SD)	2.56 (0.527)	2.50 (0.548)
			LS Mean (SE) [2]	2.55 (0.186)	2.50 (0.224)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.05 (0.291)	
			95% CI for LS Mean Difference [2]	-0.55, 0.65	
			p-value MMRM [2]	0.8643	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.09	
			95% CI for SMD (Hedges' g)	-0.95, 1.12	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C fine motor skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	11 (91.67)	6 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	2.45 (0.522)	2.00 (0.632)
			LS Mean (SE) [2]	2.45 (0.167)	2.00 (0.224)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.45 (0.279)	
			95% CI for LS Mean Difference [2]	-0.12, 1.02	
			p-value MMRM [2]	0.1204	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.78	
			95% CI for SMD (Hedges' g)	-0.26, 1.81	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.9.21 CaGI-C fine motor skills responders - any improvement by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Gender, p-value Chi-Square[1]	0.5464	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (14.29)
		Non-Responders [1]	9 (75.00)	4 (57.14)
		Responders	3 (25.00)	3 (42.86)
		OR (95% CI)	0.44 (0.06, 3.24)	
		RR (95% CI)	0.58 (0.16, 2.14)	
		RD % (95% CI)	-17.86 (-61.95, 26.24)	
		p-value – Fisher's Exact Test	0.6169	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [1]	6 (50.00)	3 (42.86)
		Responders	6 (50.00)	4 (57.14)
		OR (95% CI)	0.75 (0.11, 4.90)	
		RR (95% CI)	0.88 (0.37, 2.06)	
		RD % (95% CI)	-7.14 (-53.45, 39.16)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CaGI-C fine motor skills responders - any improvement by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (22.22)	0 (0.00)
		Non-Responders [1]	8 (88.89)	4 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	1.59 (0.05, 47.52)	
		RR (95% CI)	1.50 (0.07, 30.59)	
		RD % (95% CI)	5.00 (-29.37, 39.37)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	7 (77.78)	2 (50.00)
		Responders	2 (22.22)	2 (50.00)
		OR (95% CI)	0.29 (0.02, 3.52)	
		RR (95% CI)	0.44 (0.09, 2.13)	
		RD % (95% CI)	-27.78 (-83.80, 28.25)	
		p-value – Fisher's Exact Test	0.5301	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.9.22 CaGI-C fine motor skills responders - any improvement by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Age Group, p-value Chi-Square[1]	0.6791	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (25.00)	1 (25.00)
		Non-Responders [1]	10 (83.33)	2 (50.00)
		Responders	2 (16.67)	2 (50.00)
		OR (95% CI)	0.20 (0.02, 2.39)	
		RR (95% CI)	0.33 (0.07, 1.65)	
		RD % (95% CI)	-33.33 (-86.68, 20.01)	
		p-value – Fisher's Exact Test	0.2445	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [1]	7 (58.33)	2 (50.00)
		Responders	5 (41.67)	2 (50.00)
		OR (95% CI)	0.71 (0.07, 6.92)	
		RR (95% CI)	0.83 (0.25, 2.73)	
		RD % (95% CI)	-8.33 (-64.72, 48.05)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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CaGI-C fine motor skills responders - any improvement by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	7 (77.78)	6 (85.71)
		Responders	2 (22.22)	1 (14.29)
		OR (95% CI)	1.71 (0.12, 23.94)	
		RR (95% CI)	1.56 (0.17, 13.87)	
		RD % (95% CI)	7.94 (-29.61, 45.48)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	6 (66.67)	3 (42.86)
		Responders	3 (33.33)	4 (57.14)
		OR (95% CI)	0.38 (0.05, 2.88)	
		RR (95% CI)	0.58 (0.19, 1.80)	
		RD % (95% CI)	-23.81 (-71.69, 24.07)	
		p-value – Fisher's Exact Test	0.6145	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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4.10.9.23 CaGI-C fine motor skills responders - any improvement by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Region, p-value Chi-Square[1]	0.8123	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (12.50)	1 (16.67)
		Non-Responders [1]	6 (75.00)	3 (50.00)
		Responders	2 (25.00)	3 (50.00)
		OR (95% CI)	0.33 (0.03, 3.20)	
		RR (95% CI)	0.50 (0.12, 2.12)	
		RD % (95% CI)	-25.00 (-75.01, 25.01)	
		p-value – Fisher's Exact Test	0.5804	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	5 (62.50)	3 (50.00)
		Responders	3 (37.50)	3 (50.00)
		OR (95% CI)	0.60 (0.07, 5.14)	
		RR (95% CI)	0.75 (0.23, 2.49)	
		RD % (95% CI)	-12.50 (-64.71, 39.71)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CaGI-C fine motor skills responders - any improvement by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (23.08)	0 (0.00)
		Non-Responders [1]	11 (84.62)	5 (100.00)
		Responders	2 (15.38)	0 (0.00)
		OR (95% CI)	2.39 (0.10, 58.77)	
		RR (95% CI)	2.14 (0.12, 38.24)	
		RD % (95% CI)	9.52 (-20.34, 39.38)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (15.38)	0 (0.00)
		Non-Responders [1]	8 (61.54)	2 (40.00)
		Responders	5 (38.46)	3 (60.00)
		OR (95% CI)	0.42 (0.05, 3.43)	
		RR (95% CI)	0.64 (0.24, 1.73)	
		RD % (95% CI)	-21.54 (-71.97, 28.89)	
		p-value – Fisher's Exact Test	0.6078	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.9.24 CaGI-C fine motor skills responders - any improvement by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.3464	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (20.00)
		Non-Responders [1]	9 (100.00)	5 (100.00)
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	7 (77.78)	4 (80.00)
		Responders	2 (22.22)	1 (20.00)
		OR (95% CI)	1.14 (0.08, 16.95)	
		RR (95% CI)	1.11 (0.13, 9.42)	
		RD % (95% CI)	2.22 (-42.13, 46.57)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CaGI-C fine motor skills responders - any improvement by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (25.00)	0 (0.00)
		Non-Responders [1]	8 (66.67)	3 (50.00)
		Responders	4 (33.33)	3 (50.00)
		OR (95% CI)	0.50 (0.07, 3.70)	
		RR (95% CI)	0.67 (0.22, 2.07)	
		RD % (95% CI)	-16.67 (-64.75, 31.42)	
		p-value – Fisher's Exact Test	0.6267	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [1]	6 (50.00)	1 (16.67)
		Responders	6 (50.00)	5 (83.33)
		OR (95% CI)	0.20 (0.02, 2.26)	
		RR (95% CI)	0.60 (0.31, 1.17)	
		RD % (95% CI)	-33.33 (-74.44, 7.77)	
		p-value – Fisher's Exact Test	0.3156	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.9.25 CaGI-C gross motor skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.5271	
Male	Week 12	Absolute value	n (%)	10 (83.33)	6 (85.71)
			Number of patients with missing data: n (%)	2 (16.67)	1 (14.29)
			Mean (SD)	2.70 (0.483)	2.50 (0.548)
			LS Mean (SE) [2]	2.68 (0.156)	2.53 (0.200)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.14 (0.253)	
			95% CI for LS Mean Difference [2]	-0.39, 0.68	
			p-value MMRM [2]	0.5776	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.27	
			95% CI for SMD (Hedges' g)	-0.75, 1.29	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C gross motor skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	10 (83.33)	7 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	2.50 (0.707)	2.57 (0.535)
			LS Mean (SE) [2]	2.44 (0.204)	2.57 (0.247)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.13 (0.320)	
			95% CI for LS Mean Difference [2]	-0.81, 0.55	
			p-value MMRM [2]	0.6965	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.18	
			95% CI for SMD (Hedges' g)	-1.15, 0.79	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C gross motor skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	2.71 (0.488)	2.50 (1.000)
			LS Mean (SE) [2]	2.74 (0.225)	2.50 (0.325)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.24 (0.395)	
			95% CI for LS Mean Difference [2]	-0.62, 1.11	
			p-value MMRM [2]	0.5479	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.36	
			95% CI for SMD (Hedges' g)	-0.88, 1.60	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C gross motor skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	2.89 (0.333)	2.50 (1.000)
			LS Mean (SE) [2]	2.89 (0.198)	2.50 (0.297)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.39 (0.357)	
			95% CI for LS Mean Difference [2]	-0.40, 1.18	
			p-value MMRM [2]	0.2997	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.58	
			95% CI for SMD (Hedges' g)	-0.62, 1.79	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.9.26 CaGI-C gross motor skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.0274 ***	
<10.5 years old at screening	Week 12	Absolute value	n (%)	9 (75.00)	3 (75.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
			Mean (SD)	2.56 (0.527)	3.00 (0.000)
			LS Mean (SE) [2]	2.56 (0.152)	3.03 (0.262)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.47 (0.303)	
			95% CI for LS Mean Difference [2]	-1.14, 0.19	
			p-value MMRM [2]	0.1473	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.92	
			95% CI for SMD (Hedges' g)	-2.29, 0.44	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-C gross motor skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	2.45 (0.688)	2.75 (0.500)
			LS Mean (SE) [2]	2.45 (0.196)	2.75 (0.325)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.30 (0.379)	
			95% CI for LS Mean Difference [2]	-1.11, 0.52	
			p-value MMRM [2]	0.4496	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.41	
			95% CI for SMD (Hedges' g)	-1.57, 0.74	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-C gross motor skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	8 (88.89)	7 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.88 (0.354)	2.29 (0.756)
			LS Mean (SE) [2]	2.89 (0.189)	2.29 (0.211)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.60 (0.284)	
			95% CI for LS Mean Difference [2]	-0.01, 1.21	
			p-value MMRM [2]	0.0526	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.00	
			95% CI for SMD (Hedges' g)	-0.08, 2.09	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-C gross motor skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	8 (88.89)	7 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	3.00 (0.000)	2.43 (0.787)
			LS Mean (SE) [2]	2.90 (0.192)	2.43 (0.214)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.47 (0.288)	
			95% CI for LS Mean Difference [2]	-0.15, 1.09	
			p-value MMRM [2]	0.1247	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.77	
			95% CI for SMD (Hedges' g)	-0.28, 1.83	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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4.10.9.27 CaGI-C gross motor skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.5489	
US	Week 12	Absolute value	n (%)	7 (87.50)	5 (83.33)
			Number of patients with missing data: n (%)	1 (12.50)	1 (16.67)
			Mean (SD)	2.71 (0.488)	2.40 (0.894)
			LS Mean (SE) [2]	2.75 (0.239)	2.50 (0.278)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.26 (0.366)	
			95% CI for LS Mean Difference [2]	-0.54, 1.05	
			p-value MMRM [2]	0.4977	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.37	
			95% CI for SMD (Hedges' g)	-0.79, 1.53	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C gross motor skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	2.63 (0.744)	2.33 (0.816)
			LS Mean (SE) [2]	2.63 (0.274)	2.33 (0.316)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.29 (0.419)	
			95% CI for LS Mean Difference [2]	-0.62, 1.20	
			p-value MMRM [2]	0.4992	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.34	
			95% CI for SMD (Hedges' g)	-0.73, 1.41	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C gross motor skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	10 (76.92)	5 (100.00)
			Number of patients with missing data: n (%)	3 (23.08)	0 (0.00)
			Mean (SD)	2.70 (0.483)	2.60 (0.548)
			LS Mean (SE) [2]	2.68 (0.159)	2.60 (0.227)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.08 (0.277)	
			95% CI for LS Mean Difference [2]	-0.52, 0.68	
			p-value MMRM [2]	0.7812	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.14	
			95% CI for SMD (Hedges' g)	-0.93, 1.22	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C gross motor skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	11 (84.62)	5 (100.00)
			Number of patients with missing data: n (%)	2 (15.38)	0 (0.00)
			Mean (SD)	2.73 (0.467)	2.80 (0.447)
			LS Mean (SE) [2]	2.70 (0.140)	2.80 (0.208)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.10 (0.251)	
			95% CI for LS Mean Difference [2]	-0.64, 0.44	
			p-value MMRM [2]	0.6943	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.20	
			95% CI for SMD (Hedges' g)	-1.26, 0.86	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.9.28 CaGI-C gross motor skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.6852	
I	Week 12	Absolute value	n (%)	8 (88.89)	4 (80.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (20.00)
			Mean (SD)	2.88 (0.354)	2.50 (1.000)
			LS Mean (SE) [2]	2.87 (0.214)	2.57 (0.275)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.30 (0.348)	
			95% CI for LS Mean Difference [2]	-0.46, 1.07	
			p-value MMRM [2]	0.4040	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.46	
			95% CI for SMD (Hedges' g)	-0.76, 1.67	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C gross motor skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.75 (0.707)	2.60 (0.894)
			LS Mean (SE) [2]	2.75 (0.276)	2.60 (0.349)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.15 (0.445)	
			95% CI for LS Mean Difference [2]	-0.83, 1.13	
			p-value MMRM [2]	0.7424	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.17	
			95% CI for SMD (Hedges' g)	-0.95, 1.29	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C gross motor skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	9 (75.00)	6 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			Mean (SD)	2.56 (0.527)	2.50 (0.548)
			LS Mean (SE) [2]	2.56 (0.177)	2.50 (0.218)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.06 (0.281)	
			95% CI for LS Mean Difference [2]	-0.54, 0.67	
			p-value MMRM [2]	0.8273	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.11	
			95% CI for SMD (Hedges' g)	-0.93, 1.14	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C gross motor skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	11 (91.67)	6 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	2.64 (0.505)	2.50 (0.548)
			LS Mean (SE) [2]	2.62 (0.157)	2.50 (0.212)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.12 (0.264)	
			95% CI for LS Mean Difference [2]	-0.45, 0.68	
			p-value MMRM [2]	0.6655	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.21	
			95% CI for SMD (Hedges' g)	-0.79, 1.20	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.9.29 CaGI-C gross motor skills responders - any improvement by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Gender, p-value Chi-Square[1]	0.7557	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (14.29)
		Non-Responders [1]	9 (75.00)	4 (57.14)
		Responders	3 (25.00)	3 (42.86)
		OR (95% CI)	0.44 (0.06, 3.24)	
		RR (95% CI)	0.58 (0.16, 2.14)	
		RD % (95% CI)	-17.86 (-61.95, 26.24)	
		p-value – Fisher's Exact Test	0.6169	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [1]	8 (66.67)	4 (57.14)
		Responders	4 (33.33)	3 (42.86)
		OR (95% CI)	0.67 (0.10, 4.54)	
		RR (95% CI)	0.78 (0.24, 2.51)	
		RD % (95% CI)	-9.52 (-54.86, 35.81)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CaGI-C gross motor skills responders - any improvement by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (22.22)	0 (0.00)
		Non-Responders [1]	7 (77.78)	3 (75.00)
		Responders	2 (22.22)	1 (25.00)
		OR (95% CI)	0.86 (0.05, 13.48)	
		RR (95% CI)	0.89 (0.11, 7.20)	
		RD % (95% CI)	-2.78 (-53.16, 47.60)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	8 (88.89)	3 (75.00)
		Responders	1 (11.11)	1 (25.00)
		OR (95% CI)	0.38 (0.02, 8.10)	
		RR (95% CI)	0.44 (0.04, 5.46)	
		RD % (95% CI)	-13.89 (-61.03, 33.25)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.9.30 CaGI-C gross motor skills responders - any improvement by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Age Group, p-value Chi-Square[1]	0.9605	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (25.00)	1 (25.00)
		Non-Responders [1]	8 (66.67)	4 (100.00)
		Responders	4 (33.33)	0 (0.00)
		OR (95% CI)	4.76 (0.21, 109.78)	
		RR (95% CI)	3.46 (0.22, 53.27)	
		RD % (95% CI)	24.62 (-12.27, 61.50)	
		p-value – Fisher's Exact Test	0.5165	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [1]	7 (58.33)	3 (75.00)
		Responders	5 (41.67)	1 (25.00)
		OR (95% CI)	2.14 (0.17, 27.10)	
		RR (95% CI)	1.67 (0.27, 10.33)	
		RD % (95% CI)	16.67 (-34.11, 67.45)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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CaGI-C gross motor skills responders - any improvement by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	8 (88.89)	3 (42.86)
		Responders	1 (11.11)	4 (57.14)
		OR (95% CI)	0.09 (0.01, 1.21)	
		RR (95% CI)	0.19 (0.03, 1.38)	
		RD % (95% CI)	-46.03 (-88.05, -4.01)	
		p-value – Fisher's Exact Test	0.1058	
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	9 (100.00)	4 (57.14)
		Responders	0 (0.00)	3 (42.86)
		OR (95% CI)	0.07 (0.00, 1.61)	
		RR (95% CI)	0.11 (0.01, 1.91)	
		RD % (95% CI)	-38.75 (-75.68, -1.82)	
		p-value – Fisher's Exact Test	0.0625	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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4.10.9.31 CaGI-C gross motor skills responders - any improvement by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Region, p-value Chi-Square[1]	0.4608	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (12.50)	1 (16.67)
		Non-Responders [1]	6 (75.00)	4 (66.67)
		Responders	2 (25.00)	2 (33.33)
		OR (95% CI)	0.67 (0.06, 6.87)	
		RR (95% CI)	0.75 (0.14, 3.90)	
		RD % (95% CI)	-8.33 (-56.53, 39.87)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	6 (75.00)	3 (50.00)
		Responders	2 (25.00)	3 (50.00)
		OR (95% CI)	0.33 (0.03, 3.20)	
		RR (95% CI)	0.50 (0.12, 2.12)	
		RD % (95% CI)	-25.00 (-75.01, 25.01)	
		p-value – Fisher's Exact Test	0.5804	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CaGI-C gross motor skills responders - any improvement by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (23.08)	0 (0.00)
		Non-Responders [1]	10 (76.92)	3 (60.00)
		Responders	3 (23.08)	2 (40.00)
		OR (95% CI)	0.45 (0.05, 4.09)	
		RR (95% CI)	0.58 (0.13, 2.49)	
		RD % (95% CI)	-16.92 (-65.59, 31.74)	
		p-value – Fisher's Exact Test	0.5827	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (15.38)	0 (0.00)
		Non-Responders [1]	10 (76.92)	4 (80.00)
		Responders	3 (23.08)	1 (20.00)
		OR (95% CI)	1.20 (0.09, 15.26)	
		RR (95% CI)	1.15 (0.15, 8.65)	
		RD % (95% CI)	3.08 (-38.80, 44.96)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Table Generation: 11SEP2023 9:31:40 AM

4.10.9.32 CaGI-C gross motor skills responders - any improvement by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.9998	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (20.00)
		Non-Responders [1]	8 (88.89)	4 (80.00)
		Responders	1 (11.11)	1 (20.00)
		OR (95% CI)	0.50 (0.02, 10.25)	
		RR (95% CI)	0.56 (0.04, 7.09)	
		RD % (95% CI)	-8.89 (-49.52, 31.74)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	8 (88.89)	4 (80.00)
		Responders	1 (11.11)	1 (20.00)
		OR (95% CI)	0.50 (0.02, 10.25)	
		RR (95% CI)	0.56 (0.04, 7.09)	
		RD % (95% CI)	-8.89 (-49.52, 31.74)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Table Generation: 11SEP2023 9:31:47 AM

CaGI-C gross motor skills responders - any improvement by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (25.00)	0 (0.00)
		Non-Responders [1]	8 (66.67)	3 (50.00)
		Responders	4 (33.33)	3 (50.00)
		OR (95% CI)	0.50 (0.07, 3.70)	
		RR (95% CI)	0.67 (0.22, 2.07)	
		RD % (95% CI)	-16.67 (-64.75, 31.42)	
		p-value – Fisher's Exact Test	0.6267	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [1]	8 (66.67)	3 (50.00)
		Responders	4 (33.33)	3 (50.00)
		OR (95% CI)	0.50 (0.07, 3.70)	
		RR (95% CI)	0.67 (0.22, 2.07)	
		RD % (95% CI)	-16.67 (-64.75, 31.42)	
		p-value – Fisher's Exact Test	0.6267	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Table Generation: 11SEP2023 9:31:47 AM

4.10.9.33 CaGI-C daily living skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.8645	
Male	Week 12	Absolute value	n (%)	10 (83.33)	6 (85.71)
			Number of patients with missing data: n (%)	2 (16.67)	1 (14.29)
			Mean (SD)	2.70 (0.483)	2.67 (0.516)
			LS Mean (SE) [2]	2.68 (0.155)	2.70 (0.200)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.02 (0.253)	
			95% CI for LS Mean Difference [2]	-0.56, 0.52	
			p-value MMRM [2]	0.9508	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.03	
			95% CI for SMD (Hedges' g)	-1.04, 0.98	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C daily living skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	10 (83.33)	7 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	2.50 (0.707)	2.43 (0.535)
			LS Mean (SE) [2]	2.46 (0.204)	2.43 (0.245)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.03 (0.319)	
			95% CI for LS Mean Difference [2]	-0.65, 0.71	
			p-value MMRM [2]	0.9260	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.04	
			95% CI for SMD (Hedges' g)	-0.92, 1.01	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C daily living skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	2.57 (0.787)	3.00 (0.000)
			LS Mean (SE) [2]	2.58 (0.247)	3.00 (0.321)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.42 (0.404)	
			95% CI for LS Mean Difference [2]	-1.34, 0.49	
			p-value MMRM [2]	0.3217	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.57	
			95% CI for SMD (Hedges' g)	-1.82, 0.69	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C daily living skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	2.89 (0.333)	2.50 (1.000)
			LS Mean (SE) [2]	2.89 (0.198)	2.50 (0.297)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.39 (0.357)	
			95% CI for LS Mean Difference [2]	-0.40, 1.18	
			p-value MMRM [2]	0.2997	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.58	
			95% CI for SMD (Hedges' g)	-0.62, 1.79	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.9.34 CaGI-C daily living skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.2558	
<10.5 years old at screening	Week 12	Absolute value	n (%)	9 (75.00)	3 (75.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
			Mean (SD)	2.56 (0.726)	3.00 (0.000)
			LS Mean (SE) [2]	2.55 (0.218)	3.04 (0.379)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.49 (0.437)	
			95% CI for LS Mean Difference [2]	-1.46, 0.48	
			p-value MMRM [2]	0.2886	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.66	
			95% CI for SMD (Hedges' g)	-2.00, 0.68	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-C daily living skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	2.55 (0.688)	2.50 (0.577)
			LS Mean (SE) [2]	2.55 (0.200)	2.50 (0.332)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.05 (0.388)	
			95% CI for LS Mean Difference [2]	-0.79, 0.88	
			p-value MMRM [2]	0.9084	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.06	
			95% CI for SMD (Hedges' g)	-1.08, 1.21	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-C daily living skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	8 (88.89)	7 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.75 (0.463)	2.71 (0.488)
			LS Mean (SE) [2]	2.75 (0.169)	2.71 (0.179)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.04 (0.246)	
			95% CI for LS Mean Difference [2]	-0.49, 0.57	
			p-value MMRM [2]	0.8762	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.07	
			95% CI for SMD (Hedges' g)	-0.94, 1.09	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-C daily living skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	8 (88.89)	7 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.88 (0.354)	2.43 (0.787)
			LS Mean (SE) [2]	2.85 (0.212)	2.43 (0.225)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.42 (0.310)	
			95% CI for LS Mean Difference [2]	-0.25, 1.09	
			p-value MMRM [2]	0.1983	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.64	
			95% CI for SMD (Hedges' g)	-0.41, 1.68	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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4.10.9.35 CaGI-C daily living skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.2967	
US	Week 12	Absolute value	n (%)	7 (87.50)	5 (83.33)
			Number of patients with missing data: n (%)	1 (12.50)	1 (16.67)
			Mean (SD)	2.57 (0.787)	2.80 (0.447)
			LS Mean (SE) [2]	2.58 (0.257)	2.83 (0.305)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.26 (0.399)	
			95% CI for LS Mean Difference [2]	-1.15, 0.63	
			p-value MMRM [2]	0.5320	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.33	
			95% CI for SMD (Hedges' g)	-1.49, 0.82	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C daily living skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	2.88 (0.354)	2.17 (0.753)
			LS Mean (SE) [2]	2.87 (0.197)	2.17 (0.227)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.71 (0.300)	
			95% CI for LS Mean Difference [2]	0.05, 1.36	
			p-value MMRM [2]	0.0361 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.15	
			95% CI for SMD (Hedges' g)	-0.01, 2.30	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C daily living skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	10 (76.92)	5 (100.00)
			Number of patients with missing data: n (%)	3 (23.08)	0 (0.00)
			Mean (SD)	2.70 (0.483)	2.80 (0.447)
			LS Mean (SE) [2]	2.70 (0.145)	2.80 (0.209)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.10 (0.255)	
			95% CI for LS Mean Difference [2]	-0.65, 0.45	
			p-value MMRM [2]	0.7016	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.20	
			95% CI for SMD (Hedges' g)	-1.27, 0.88	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C daily living skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	11 (84.62)	5 (100.00)
			Number of patients with missing data: n (%)	2 (15.38)	0 (0.00)
			Mean (SD)	2.55 (0.688)	2.80 (0.447)
			LS Mean (SE) [2]	2.50 (0.191)	2.80 (0.286)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.30 (0.344)	
			95% CI for LS Mean Difference [2]	-1.04, 0.44	
			p-value MMRM [2]	0.3923	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.44	
			95% CI for SMD (Hedges' g)	-1.51, 0.63	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.9.36 CaGI-C daily living skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.8417	
I	Week 12	Absolute value	n (%)	8 (88.89)	4 (80.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (20.00)
			Mean (SD)	2.88 (0.354)	3.00 (0.000)
			LS Mean (SE) [2]	2.88 (0.104)	3.02 (0.146)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.15 (0.179)	
			95% CI for LS Mean Difference [2]	-0.54, 0.25	
			p-value MMRM [2]	0.4289	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.44	
			95% CI for SMD (Hedges' g)	-1.66, 0.77	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C daily living skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.88 (0.354)	2.60 (0.894)
			LS Mean (SE) [2]	2.87 (0.215)	2.60 (0.272)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.27 (0.347)	
			95% CI for LS Mean Difference [2]	-0.49, 1.04	
			p-value MMRM [2]	0.4448	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.40	
			95% CI for SMD (Hedges' g)	-0.73, 1.53	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C daily living skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	9 (75.00)	6 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			Mean (SD)	2.44 (0.726)	2.67 (0.516)
			LS Mean (SE) [2]	2.45 (0.221)	2.67 (0.267)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.22 (0.347)	
			95% CI for LS Mean Difference [2]	-0.97, 0.53	
			p-value MMRM [2]	0.5414	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.30	
			95% CI for SMD (Hedges' g)	-1.34, 0.74	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C daily living skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	11 (91.67)	6 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	2.55 (0.688)	2.33 (0.516)
			LS Mean (SE) [2]	2.54 (0.193)	2.33 (0.259)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.21 (0.323)	
			95% CI for LS Mean Difference [2]	-0.48, 0.90	
			p-value MMRM [2]	0.5303	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.30	
			95% CI for SMD (Hedges' g)	-0.70, 1.30	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.9.37 CaGI-C daily living skills responders - any improvement by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Gender, p-value Chi-Square[1]	1.0000	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (14.29)
		Non-Responders [1]	9 (75.00)	5 (71.43)
		Responders	3 (25.00)	2 (28.57)
		OR (95% CI)	0.83 (0.10, 6.78)	
		RR (95% CI)	0.88 (0.19, 4.03)	
		RD % (95% CI)	-3.57 (-45.05, 37.90)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [1]	8 (66.67)	3 (42.86)
		Responders	4 (33.33)	4 (57.14)
		OR (95% CI)	0.38 (0.06, 2.55)	
		RR (95% CI)	0.58 (0.21, 1.63)	
		RD % (95% CI)	-23.81 (-69.15, 21.53)	
		p-value – Fisher's Exact Test	0.3765	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CaGI-C daily living skills responders - any improvement by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (22.22)	0 (0.00)
		Non-Responders [1]	7 (77.78)	4 (100.00)
		Responders	2 (22.22)	0 (0.00)
		OR (95% CI)	3.00 (0.12, 77.64)	
		RR (95% CI)	2.50 (0.15, 42.80)	
		RD % (95% CI)	15.00 (-22.57, 52.57)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	8 (88.89)	3 (75.00)
		Responders	1 (11.11)	1 (25.00)
		OR (95% CI)	0.38 (0.02, 8.10)	
		RR (95% CI)	0.44 (0.04, 5.46)	
		RD % (95% CI)	-13.89 (-61.03, 33.25)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.9.38 CaGI-C daily living skills responders - any improvement by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Age Group, p-value Chi-Square[1]	0.5315	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (25.00)	1 (25.00)
		Non-Responders [1]	9 (75.00)	4 (100.00)
		Responders	3 (25.00)	0 (0.00)
		OR (95% CI)	3.32 (0.14, 78.81)	
		RR (95% CI)	2.69 (0.17, 43.31)	
		RD % (95% CI)	16.92 (-18.75, 52.60)	
		p-value – Fisher's Exact Test	0.5286	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [1]	8 (66.67)	2 (50.00)
		Responders	4 (33.33)	2 (50.00)
		OR (95% CI)	0.50 (0.05, 4.98)	
		RR (95% CI)	0.67 (0.19, 2.36)	
		RD % (95% CI)	-16.67 (-72.45, 39.12)	
		p-value – Fisher's Exact Test	0.6044	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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CaGI-C daily living skills responders - any improvement by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	7 (77.78)	5 (71.43)
		Responders	2 (22.22)	2 (28.57)
		OR (95% CI)	0.71 (0.07, 6.92)	
		RR (95% CI)	0.78 (0.14, 4.23)	
		RD % (95% CI)	-6.35 (-49.45, 36.75)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	8 (88.89)	4 (57.14)
		Responders	1 (11.11)	3 (42.86)
		OR (95% CI)	0.17 (0.01, 2.16)	
		RR (95% CI)	0.26 (0.03, 1.99)	
		RD % (95% CI)	-31.75 (-73.76, 10.27)	
		p-value – Fisher's Exact Test	0.2615	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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4.10.9.39 CaGI-C daily living skills responders - any improvement by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Region, p-value Chi-Square[1]	0.0860	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (12.50)	1 (16.67)
		Non-Responders [1]	6 (75.00)	5 (83.33)
		Responders	2 (25.00)	1 (16.67)
		OR (95% CI)	1.67 (0.11, 24.26)	
		RR (95% CI)	1.50 (0.17, 12.94)	
		RD % (95% CI)	8.33 (-33.97, 50.64)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	7 (87.50)	2 (33.33)
		Responders	1 (12.50)	4 (66.67)
		OR (95% CI)	0.07 (0.00, 1.06)	
		RR (95% CI)	0.19 (0.03, 1.28)	
		RD % (95% CI)	-54.17 (-98.30, -10.03)	
		p-value – Fisher's Exact Test	0.0909	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CaGI-C daily living skills responders - any improvement by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (23.08)	0 (0.00)
		Non-Responders [1]	10 (76.92)	4 (80.00)
		Responders	3 (23.08)	1 (20.00)
		OR (95% CI)	1.20 (0.09, 15.26)	
		RR (95% CI)	1.15 (0.15, 8.65)	
		RD % (95% CI)	3.08 (-38.80, 44.96)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (15.38)	0 (0.00)
		Non-Responders [1]	9 (69.23)	4 (80.00)
		Responders	4 (30.77)	1 (20.00)
		OR (95% CI)	1.78 (0.15, 21.39)	
		RR (95% CI)	1.54 (0.22, 10.64)	
		RD % (95% CI)	10.77 (-32.34, 53.88)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.9.40 CaGI-C daily living skills responders - any improvement by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.7110	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (20.00)
		Non-Responders [1]	8 (88.89)	5 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	1.94 (0.07, 56.76)	
		RR (95% CI)	1.80 (0.09, 37.49)	
		RD % (95% CI)	6.67 (-24.62, 37.95)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	8 (88.89)	4 (80.00)
		Responders	1 (11.11)	1 (20.00)
		OR (95% CI)	0.50 (0.02, 10.25)	
		RR (95% CI)	0.56 (0.04, 7.09)	
		RD % (95% CI)	-8.89 (-49.52, 31.74)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CaGI-C daily living skills responders - any improvement by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (25.00)	0 (0.00)
		Non-Responders [1]	8 (66.67)	4 (66.67)
		Responders	4 (33.33)	2 (33.33)
		OR (95% CI)	1.00 (0.13, 8.00)	
		RR (95% CI)	1.00 (0.25, 4.00)	
		RD % (95% CI)	0.00 (-46.20, 46.20)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [1]	8 (66.67)	2 (33.33)
		Responders	4 (33.33)	4 (66.67)
		OR (95% CI)	0.25 (0.03, 2.00)	
		RR (95% CI)	0.50 (0.19, 1.33)	
		RD % (95% CI)	-33.33 (-79.53, 12.86)	
		p-value – Fisher's Exact Test	0.3213	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.9.41 CaGI-C communication skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.4658	
Male	Week 12	Absolute value	n (%)	10 (83.33)	6 (85.71)
			Number of patients with missing data: n (%)	2 (16.67)	1 (14.29)
			Mean (SD)	2.40 (0.516)	2.33 (0.816)
			LS Mean (SE) [2]	2.31 (0.206)	2.41 (0.262)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.10 (0.333)	
			95% CI for LS Mean Difference [2]	-0.81, 0.61	
			p-value MMRM [2]	0.7672	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.14	
			95% CI for SMD (Hedges' g)	-1.16, 0.87	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C communication skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	10 (83.33)	7 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	2.30 (0.823)	2.29 (0.756)
			LS Mean (SE) [2]	2.27 (0.241)	2.29 (0.297)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.02 (0.382)	
			95% CI for LS Mean Difference [2]	-0.83, 0.80	
			p-value MMRM [2]	0.9691	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.02	
			95% CI for SMD (Hedges' g)	-0.98, 0.95	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C communication skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	2.71 (0.488)	2.75 (0.500)
			LS Mean (SE) [2]	2.72 (0.187)	2.75 (0.244)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.03 (0.307)	
			95% CI for LS Mean Difference [2]	-0.72, 0.66	
			p-value MMRM [2]	0.9299	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.05	
			95% CI for SMD (Hedges' g)	-1.28, 1.18	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C communication skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	2.89 (0.333)	2.00 (0.816)
			LS Mean (SE) [2]	2.89 (0.171)	2.00 (0.256)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.89 (0.308)	
			95% CI for LS Mean Difference [2]	0.21, 1.57	
			p-value MMRM [2]	0.0148 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.54	
			95% CI for SMD (Hedges' g)	0.20, 2.89	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.9.42 CaGI-C communication skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.7361	
<10.5 years old at screening	Week 12	Absolute value	n (%)	9 (75.00)	3 (75.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
			Mean (SD)	2.56 (0.527)	2.33 (0.577)
			LS Mean (SE) [2]	2.50 (0.186)	2.50 (0.314)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.00 (0.365)	
			95% CI for LS Mean Difference [2]	-0.80, 0.81	
			p-value MMRM [2]	0.9902	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.01	
			95% CI for SMD (Hedges' g)	-1.30, 1.31	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-C communication skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	2.36 (0.809)	2.25 (0.500)
			LS Mean (SE) [2]	2.36 (0.226)	2.25 (0.375)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.11 (0.437)	
			95% CI for LS Mean Difference [2]	-0.83, 1.06	
			p-value MMRM [2]	0.7991	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.14	
			95% CI for SMD (Hedges' g)	-1.01, 1.28	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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CaGI-C communication skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	8 (88.89)	7 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.50 (0.535)	2.57 (0.787)
			LS Mean (SE) [2]	2.51 (0.230)	2.57 (0.248)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.06 (0.339)	
			95% CI for LS Mean Difference [2]	-0.79, 0.67	
			p-value MMRM [2]	0.8591	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.09	
			95% CI for SMD (Hedges' g)	-1.10, 0.93	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-C communication skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	8 (88.89)	7 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.88 (0.354)	2.14 (0.900)
			LS Mean (SE) [2]	2.84 (0.232)	2.14 (0.250)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.70 (0.341)	
			95% CI for LS Mean Difference [2]	-0.04, 1.43	
			p-value MMRM [2]	0.0606	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.97	
			95% CI for SMD (Hedges' g)	-0.11, 2.05	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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4.10.9.43 CaGI-C communication skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.5837	
US	Week 12	Absolute value	n (%)	7 (87.50)	5 (83.33)
			Number of patients with missing data: n (%)	1 (12.50)	1 (16.67)
			Mean (SD)	2.57 (0.535)	2.40 (0.894)
			LS Mean (SE) [2]	2.61 (0.261)	2.51 (0.307)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.10 (0.403)	
			95% CI for LS Mean Difference [2]	-0.79, 0.99	
			p-value MMRM [2]	0.8110	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.13	
			95% CI for SMD (Hedges' g)	-1.02, 1.28	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C communication skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	2.50 (0.756)	2.00 (0.894)
			LS Mean (SE) [2]	2.50 (0.289)	2.00 (0.333)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.50 (0.441)	
			95% CI for LS Mean Difference [2]	-0.46, 1.46	
			p-value MMRM [2]	0.2790	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.55	
			95% CI for SMD (Hedges' g)	-0.53, 1.63	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C communication skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	10 (76.92)	5 (100.00)
			Number of patients with missing data: n (%)	3 (23.08)	0 (0.00)
			Mean (SD)	2.50 (0.527)	2.60 (0.548)
			LS Mean (SE) [2]	2.42 (0.183)	2.60 (0.268)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.18 (0.325)	
			95% CI for LS Mean Difference [2]	-0.90, 0.54	
			p-value MMRM [2]	0.5855	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.28	
			95% CI for SMD (Hedges' g)	-1.36, 0.80	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C communication skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	11 (84.62)	5 (100.00)
			Number of patients with missing data: n (%)	2 (15.38)	0 (0.00)
			Mean (SD)	2.64 (0.674)	2.40 (0.548)
			LS Mean (SE) [2]	2.61 (0.188)	2.40 (0.284)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.21 (0.341)	
			95% CI for LS Mean Difference [2]	-0.52, 0.93	
			p-value MMRM [2]	0.5521	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.30	
			95% CI for SMD (Hedges' g)	-0.76, 1.37	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.9.44 CaGI-C communication skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.5878	
I	Week 12	Absolute value	n (%)	8 (88.89)	4 (80.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (20.00)
			Mean (SD)	2.88 (0.354)	3.00 (0.000)
			LS Mean (SE) [2]	2.88 (0.104)	3.04 (0.140)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.17 (0.174)	
			95% CI for LS Mean Difference [2]	-0.55, 0.22	
			p-value MMRM [2]	0.3580	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.51	
			95% CI for SMD (Hedges' g)	-1.73, 0.71	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C communication skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.75 (0.707)	2.40 (0.894)
			LS Mean (SE) [2]	2.75 (0.276)	2.40 (0.349)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.35 (0.445)	
			95% CI for LS Mean Difference [2]	-0.63, 1.33	
			p-value MMRM [2]	0.4481	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.40	
			95% CI for SMD (Hedges' g)	-0.73, 1.53	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C communication skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	9 (75.00)	6 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			Mean (SD)	2.22 (0.441)	2.17 (0.753)
			LS Mean (SE) [2]	2.20 (0.197)	2.17 (0.256)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.03 (0.323)	
			95% CI for LS Mean Difference [2]	-0.67, 0.73	
			p-value MMRM [2]	0.9280	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.04	
			95% CI for SMD (Hedges' g)	-0.99, 1.08	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C communication skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	11 (91.67)	6 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	2.45 (0.688)	2.00 (0.632)
			LS Mean (SE) [2]	2.44 (0.194)	2.00 (0.269)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.44 (0.332)	
			95% CI for LS Mean Difference [2]	-0.26, 1.14	
			p-value MMRM [2]	0.2032	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.63	
			95% CI for SMD (Hedges' g)	-0.39, 1.65	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.9.45 CaGI-C communication skills responders - any improvement by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Gender, p-value Chi-Square[1]	0.1651	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (14.29)
		Non-Responders [1]	6 (50.00)	4 (57.14)
		Responders	6 (50.00)	3 (42.86)
		OR (95% CI)	1.33 (0.20, 8.71)	
		RR (95% CI)	1.17 (0.42, 3.25)	
		RD % (95% CI)	7.14 (-39.16, 53.45)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [1]	7 (58.33)	3 (42.86)
		Responders	5 (41.67)	4 (57.14)
		OR (95% CI)	0.54 (0.08, 3.53)	
		RR (95% CI)	0.73 (0.29, 1.84)	
		RD % (95% CI)	-15.48 (-61.54, 30.59)	
		p-value – Fisher's Exact Test	0.6499	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CaGI-C communication skills responders - any improvement by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (22.22)	0 (0.00)
		Non-Responders [1]	7 (77.78)	3 (75.00)
		Responders	2 (22.22)	1 (25.00)
		OR (95% CI)	0.86 (0.05, 13.48)	
		RR (95% CI)	0.89 (0.11, 7.20)	
		RD % (95% CI)	-2.78 (-53.16, 47.60)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	8 (88.89)	1 (25.00)
		Responders	1 (11.11)	3 (75.00)
		OR (95% CI)	0.04 (0.00, 0.90)	
		RR (95% CI)	0.15 (0.02, 1.02)	
		RD % (95% CI)	-63.89 (-100.00, -16.75)	
		p-value – Fisher's Exact Test	0.0517	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.9.46 CaGI-C communication skills responders - any improvement by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Age Group, p-value Chi-Square[1]	0.6124	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (25.00)	1 (25.00)
		Non-Responders [1]	8 (66.67)	2 (50.00)
		Responders	4 (33.33)	2 (50.00)
		OR (95% CI)	0.50 (0.05, 4.98)	
		RR (95% CI)	0.67 (0.19, 2.36)	
		RD % (95% CI)	-16.67 (-72.45, 39.12)	
		p-value – Fisher's Exact Test	0.6044	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [1]	7 (58.33)	1 (25.00)
		Responders	5 (41.67)	3 (75.00)
		OR (95% CI)	0.24 (0.02, 3.01)	
		RR (95% CI)	0.56 (0.23, 1.33)	
		RD % (95% CI)	-33.33 (-84.11, 17.45)	
		p-value – Fisher's Exact Test	0.5692	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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CaGI-C communication skills responders - any improvement by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	5 (55.56)	5 (71.43)
		Responders	4 (44.44)	2 (28.57)
		OR (95% CI)	2.00 (0.24, 16.36)	
		RR (95% CI)	1.56 (0.39, 6.19)	
		RD % (95% CI)	15.87 (-30.75, 62.50)	
		p-value – Fisher's Exact Test	0.6329	
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	8 (88.89)	3 (42.86)
		Responders	1 (11.11)	4 (57.14)
		OR (95% CI)	0.09 (0.01, 1.21)	
		RR (95% CI)	0.19 (0.03, 1.38)	
		RD % (95% CI)	-46.03 (-88.05, -4.01)	
		p-value – Fisher's Exact Test	0.1058	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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4.10.9.47 CaGI-C communication skills responders - any improvement by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Region, p-value Chi-Square[1]	0.7996	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (12.50)	1 (16.67)
		Non-Responders [1]	5 (62.50)	4 (66.67)
		Responders	3 (37.50)	2 (33.33)
		OR (95% CI)	1.20 (0.13, 11.05)	
		RR (95% CI)	1.13 (0.27, 4.76)	
		RD % (95% CI)	4.17 (-46.31, 54.65)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	5 (62.50)	2 (33.33)
		Responders	3 (37.50)	4 (66.67)
		OR (95% CI)	0.30 (0.03, 2.76)	
		RR (95% CI)	0.56 (0.20, 1.62)	
		RD % (95% CI)	-29.17 (-79.65, 21.31)	
		p-value – Fisher's Exact Test	0.5921	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CaGI-C communication skills responders - any improvement by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (23.08)	0 (0.00)
		Non-Responders [1]	8 (61.54)	3 (60.00)
		Responders	5 (38.46)	2 (40.00)
		OR (95% CI)	0.94 (0.11, 7.73)	
		RR (95% CI)	0.96 (0.27, 3.44)	
		RD % (95% CI)	-1.54 (-51.97, 48.89)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (15.38)	0 (0.00)
		Non-Responders [1]	10 (76.92)	2 (40.00)
		Responders	3 (23.08)	3 (60.00)
		OR (95% CI)	0.20 (0.02, 1.82)	
		RR (95% CI)	0.38 (0.11, 1.31)	
		RD % (95% CI)	-36.92 (-85.59, 11.74)	
		p-value – Fisher's Exact Test	0.2682	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.9.48 CaGI-C communication skills responders - any improvement by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.8844	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (20.00)
		Non-Responders [1]	8 (88.89)	5 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	1.94 (0.07, 56.76)	
		RR (95% CI)	1.80 (0.09, 37.49)	
		RD % (95% CI)	6.67 (-24.62, 37.95)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	8 (88.89)	3 (60.00)
		Responders	1 (11.11)	2 (40.00)
		OR (95% CI)	0.19 (0.01, 2.91)	
		RR (95% CI)	0.28 (0.03, 2.35)	
		RD % (95% CI)	-28.89 (-76.49, 18.71)	
		p-value – Fisher's Exact Test	0.5055	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CaGI-C communication skills responders - any improvement by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (25.00)	0 (0.00)
		Non-Responders [1]	5 (41.67)	2 (33.33)
		Responders	7 (58.33)	4 (66.67)
		OR (95% CI)	0.70 (0.09, 5.43)	
		RR (95% CI)	0.88 (0.42, 1.84)	
		RD % (95% CI)	-8.33 (-55.25, 38.58)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [1]	7 (58.33)	1 (16.67)
		Responders	5 (41.67)	5 (83.33)
		OR (95% CI)	0.14 (0.01, 1.63)	
		RR (95% CI)	0.50 (0.23, 1.07)	
		RD % (95% CI)	-41.67 (-82.50, -0.83)	
		p-value – Fisher's Exact Test	0.1516	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.9.49 CaGI-C socialization skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.0337 ***	
Male	Week 12	Absolute value	n (%)	10 (83.33)	6 (85.71)
			Number of patients with missing data: n (%)	2 (16.67)	1 (14.29)
			Mean (SD)	2.60 (0.516)	2.83 (0.408)
			LS Mean (SE) [2]	2.60 (0.153)	2.84 (0.198)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.24 (0.250)	
			95% CI for LS Mean Difference [2]	-0.78, 0.30	
			p-value MMRM [2]	0.3536	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.45	
			95% CI for SMD (Hedges' g)	-1.48, 0.57	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C socialization skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	10 (83.33)	7 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	2.50 (0.707)	2.71 (0.488)
			LS Mean (SE) [2]	2.49 (0.200)	2.71 (0.238)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.22 (0.311)	
			95% CI for LS Mean Difference [2]	-0.88, 0.44	
			p-value MMRM [2]	0.4871	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.32	
			95% CI for SMD (Hedges' g)	-1.30, 0.65	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C socialization skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	2.57 (0.787)	2.25 (0.957)
			LS Mean (SE) [2]	2.57 (0.327)	2.25 (0.424)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.32 (0.535)	
			95% CI for LS Mean Difference [2]	-0.89, 1.53	
			p-value MMRM [2]	0.5627	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.32	
			95% CI for SMD (Hedges' g)	-0.91, 1.56	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C socialization skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	3.00 (0.000)	2.25 (0.957)
			LS Mean (SE) [2]	3.00 (0.167)	2.25 (0.250)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.75 (0.300)	
			95% CI for LS Mean Difference [2]	0.09, 1.41	
			p-value MMRM [2]	0.0297 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.34	
			95% CI for SMD (Hedges' g)	0.03, 2.64	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.9.50 CaGI-C socialization skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.2315	
<10.5 years old at screening	Week 12	Absolute value	n (%)	9 (75.00)	3 (75.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
			Mean (SD)	2.56 (0.726)	2.33 (1.155)
			LS Mean (SE) [2]	2.56 (0.281)	2.33 (0.489)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.22 (0.564)	
			95% CI for LS Mean Difference [2]	-1.03, 1.48	
			p-value MMRM [2]	0.6987	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.23	
			95% CI for SMD (Hedges' g)	-1.08, 1.55	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-C socialization skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	2.64 (0.674)	3.00 (0.000)
			LS Mean (SE) [2]	2.64 (0.178)	3.00 (0.296)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.36 (0.345)	
			95% CI for LS Mean Difference [2]	-1.11, 0.38	
			p-value MMRM [2]	0.3114	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.56	
			95% CI for SMD (Hedges' g)	-1.72, 0.61	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-C socialization skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	8 (88.89)	7 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.63 (0.518)	2.71 (0.488)
			LS Mean (SE) [2]	2.63 (0.177)	2.71 (0.190)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.08 (0.260)	
			95% CI for LS Mean Difference [2]	-0.64, 0.48	
			p-value MMRM [2]	0.7541	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.15	
			95% CI for SMD (Hedges' g)	-1.17, 0.87	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-C socialization skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	8 (88.89)	7 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.88 (0.354)	2.29 (0.756)
			LS Mean (SE) [2]	2.84 (0.204)	2.29 (0.218)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.56 (0.299)	
			95% CI for LS Mean Difference [2]	-0.09, 1.20	
			p-value MMRM [2]	0.0857	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.87	
			95% CI for SMD (Hedges' g)	-0.20, 1.94	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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4.10.9.51 CaGI-C socialization skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.4818	
US	Week 12	Absolute value	n (%)	7 (87.50)	5 (83.33)
			Number of patients with missing data: n (%)	1 (12.50)	1 (16.67)
			Mean (SD)	2.57 (0.787)	2.60 (0.548)
			LS Mean (SE) [2]	2.58 (0.267)	2.61 (0.317)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.03 (0.414)	
			95% CI for LS Mean Difference [2]	-0.95, 0.89	
			p-value MMRM [2]	0.9431	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.04	
			95% CI for SMD (Hedges' g)	-1.19, 1.11	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C socialization skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	2.63 (0.744)	2.67 (0.816)
			LS Mean (SE) [2]	2.63 (0.274)	2.67 (0.316)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.04 (0.419)	
			95% CI for LS Mean Difference [2]	-0.95, 0.87	
			p-value MMRM [2]	0.9223	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.05	
			95% CI for SMD (Hedges' g)	-1.11, 1.01	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C socialization skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	10 (76.92)	5 (100.00)
			Number of patients with missing data: n (%)	3 (23.08)	0 (0.00)
			Mean (SD)	2.60 (0.516)	2.60 (0.894)
			LS Mean (SE) [2]	2.62 (0.211)	2.60 (0.294)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.02 (0.362)	
			95% CI for LS Mean Difference [2]	-0.77, 0.80	
			p-value MMRM [2]	0.9671	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.02	
			95% CI for SMD (Hedges' g)	-1.05, 1.09	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C socialization skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	11 (84.62)	5 (100.00)
			Number of patients with missing data: n (%)	2 (15.38)	0 (0.00)
			Mean (SD)	2.82 (0.405)	2.40 (0.548)
			LS Mean (SE) [2]	2.82 (0.137)	2.40 (0.201)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.42 (0.243)	
			95% CI for LS Mean Difference [2]	-0.10, 0.95	
			p-value MMRM [2]	0.1030	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.86	
			95% CI for SMD (Hedges' g)	-0.25, 1.96	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.9.52 CaGI-C socialization skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.4420	
I	Week 12	Absolute value	n (%)	8 (88.89)	4 (80.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (20.00)
			Mean (SD)	2.88 (0.354)	2.75 (0.500)
			LS Mean (SE) [2]	2.88 (0.142)	2.77 (0.203)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.10 (0.248)	
			95% CI for LS Mean Difference [2]	-0.45, 0.65	
			p-value MMRM [2]	0.6920	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.22	
			95% CI for SMD (Hedges' g)	-0.98, 1.42	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C socialization skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.75 (0.707)	2.40 (0.894)
			LS Mean (SE) [2]	2.75 (0.276)	2.40 (0.349)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.35 (0.445)	
			95% CI for LS Mean Difference [2]	-0.63, 1.33	
			p-value MMRM [2]	0.4481	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.40	
			95% CI for SMD (Hedges' g)	-0.73, 1.53	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C socialization skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	9 (75.00)	6 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			Mean (SD)	2.33 (0.707)	2.50 (0.837)
			LS Mean (SE) [2]	2.33 (0.258)	2.50 (0.310)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.17 (0.403)	
			95% CI for LS Mean Difference [2]	-1.04, 0.71	
			p-value MMRM [2]	0.6891	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.19	
			95% CI for SMD (Hedges' g)	-1.23, 0.84	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C socialization skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	11 (91.67)	6 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	2.73 (0.467)	2.67 (0.516)
			LS Mean (SE) [2]	2.73 (0.147)	2.67 (0.198)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.06 (0.246)	
			95% CI for LS Mean Difference [2]	-0.46, 0.59	
			p-value MMRM [2]	0.8058	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.12	
			95% CI for SMD (Hedges' g)	-0.88, 1.11	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.9.53 CaGI-C socialization skills responders - any improvement by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Gender, p-value Chi-Square[1]	0.9626	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (14.29)
		Non-Responders [1]	8 (66.67)	6 (85.71)
		Responders	4 (33.33)	1 (14.29)
		OR (95% CI)	3.00 (0.26, 34.20)	
		RR (95% CI)	2.33 (0.32, 16.95)	
		RD % (95% CI)	19.05 (-18.15, 56.24)	
		p-value – Fisher's Exact Test	0.6027	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [1]	8 (66.67)	5 (71.43)
		Responders	4 (33.33)	2 (28.57)
		OR (95% CI)	1.25 (0.16, 9.54)	
		RR (95% CI)	1.17 (0.28, 4.82)	
		RD % (95% CI)	4.76 (-38.03, 47.56)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CaGI-C socialization skills responders - any improvement by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (22.22)	0 (0.00)
		Non-Responders [1]	7 (77.78)	2 (50.00)
		Responders	2 (22.22)	2 (50.00)
		OR (95% CI)	0.29 (0.02, 3.52)	
		RR (95% CI)	0.44 (0.09, 2.13)	
		RD % (95% CI)	-27.78 (-83.80, 28.25)	
		p-value – Fisher's Exact Test	0.5301	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	9 (100.00)	2 (50.00)
		Responders	0 (0.00)	2 (50.00)
		OR (95% CI)	0.05 (0.00, 1.49)	
		RR (95% CI)	0.10 (0.01, 1.71)	
		RD % (95% CI)	-45.00 (-90.86, 0.86)	
		p-value – Fisher's Exact Test	0.0769	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.9.54 CaGI-C socialization skills responders - any improvement by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Age Group, p-value Chi-Square[1]	0.9732	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (25.00)	1 (25.00)
		Non-Responders [1]	9 (75.00)	3 (75.00)
		Responders	3 (25.00)	1 (25.00)
		OR (95% CI)	1.00 (0.07, 13.64)	
		RR (95% CI)	1.00 (0.14, 7.10)	
		RD % (95% CI)	0.00 (-49.00, 49.00)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [1]	9 (75.00)	4 (100.00)
		Responders	3 (25.00)	0 (0.00)
		OR (95% CI)	3.32 (0.14, 78.81)	
		RR (95% CI)	2.69 (0.17, 43.31)	
		RD % (95% CI)	16.92 (-18.75, 52.60)	
		p-value – Fisher's Exact Test	0.5286	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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CaGI-C socialization skills responders - any improvement by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	6 (66.67)	5 (71.43)
		Responders	3 (33.33)	2 (28.57)
		OR (95% CI)	1.25 (0.15, 10.70)	
		RR (95% CI)	1.17 (0.26, 5.19)	
		RD % (95% CI)	4.76 (-40.72, 50.24)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	8 (88.89)	3 (42.86)
		Responders	1 (11.11)	4 (57.14)
		OR (95% CI)	0.09 (0.01, 1.21)	
		RR (95% CI)	0.19 (0.03, 1.38)	
		RD % (95% CI)	-46.03 (-88.05, -4.01)	
		p-value – Fisher's Exact Test	0.1058	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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4.10.9.55 CaGI-C socialization skills responders - any improvement by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Region, p-value Chi-Square[1]	0.1485	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (12.50)	1 (16.67)
		Non-Responders [1]	6 (75.00)	4 (66.67)
		Responders	2 (25.00)	2 (33.33)
		OR (95% CI)	0.67 (0.06, 6.87)	
		RR (95% CI)	0.75 (0.14, 3.90)	
		RD % (95% CI)	-8.33 (-56.53, 39.87)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	6 (75.00)	5 (83.33)
		Responders	2 (25.00)	1 (16.67)
		OR (95% CI)	1.67 (0.11, 24.26)	
		RR (95% CI)	1.50 (0.17, 12.94)	
		RD % (95% CI)	8.33 (-33.97, 50.64)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CaGI-C socialization skills responders - any improvement by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (23.08)	0 (0.00)
		Non-Responders [1]	9 (69.23)	4 (80.00)
		Responders	4 (30.77)	1 (20.00)
		OR (95% CI)	1.78 (0.15, 21.39)	
		RR (95% CI)	1.54 (0.22, 10.64)	
		RD % (95% CI)	10.77 (-32.34, 53.88)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (15.38)	0 (0.00)
		Non-Responders [1]	11 (84.62)	2 (40.00)
		Responders	2 (15.38)	3 (60.00)
		OR (95% CI)	0.12 (0.01, 1.26)	
		RR (95% CI)	0.26 (0.06, 1.11)	
		RD % (95% CI)	-44.62 (-91.82, 2.59)	
		p-value – Fisher's Exact Test	0.0987	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.9.56 CaGI-C socialization skills responders - any improvement by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.4750	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (20.00)
		Non-Responders [1]	8 (88.89)	4 (80.00)
		Responders	1 (11.11)	1 (20.00)
		OR (95% CI)	0.50 (0.02, 10.25)	
		RR (95% CI)	0.56 (0.04, 7.09)	
		RD % (95% CI)	-8.89 (-49.52, 31.74)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	8 (88.89)	3 (60.00)
		Responders	1 (11.11)	2 (40.00)
		OR (95% CI)	0.19 (0.01, 2.91)	
		RR (95% CI)	0.28 (0.03, 2.35)	
		RD % (95% CI)	-28.89 (-76.49, 18.71)	
		p-value – Fisher's Exact Test	0.5055	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Program: t-qs-categ-cagic-sub.sas
Table Generation: 11SEP2023 9:33:03 AM

CaGI-C socialization skills responders - any improvement by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (25.00)	0 (0.00)
		Non-Responders [1]	7 (58.33)	4 (66.67)
		Responders	5 (41.67)	2 (33.33)
		OR (95% CI)	1.43 (0.18, 11.09)	
		RR (95% CI)	1.25 (0.34, 4.65)	
		RD % (95% CI)	8.33 (-38.58, 55.25)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [1]	9 (75.00)	4 (66.67)
		Responders	3 (25.00)	2 (33.33)
		OR (95% CI)	0.67 (0.08, 5.68)	
		RR (95% CI)	0.75 (0.17, 3.35)	
		RD % (95% CI)	-8.33 (-53.31, 36.64)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Table Generation: 11SEP2023 9:33:03 AM

4.10.9.57 CaGI-C ability to adapt to environment by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.3100	
Male	Week 12	Absolute value	n (%)	10 (83.33)	6 (85.71)
			Number of patients with missing data: n (%)	2 (16.67)	1 (14.29)
			Mean (SD)	2.60 (0.516)	2.33 (0.516)
			LS Mean (SE) [2]	2.59 (0.162)	2.36 (0.210)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.23 (0.265)	
			95% CI for LS Mean Difference [2]	-0.34, 0.79	
			p-value MMRM [2]	0.4094	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.40	
			95% CI for SMD (Hedges' g)	-0.62, 1.43	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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Table Generation: 11SEP2023 12:55:14 PM

CaGI-C ability to adapt to environment by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	10 (83.33)	7 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	2.40 (0.699)	2.43 (0.535)
			LS Mean (SE) [2]	2.37 (0.202)	2.43 (0.242)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.06 (0.315)	
			95% CI for LS Mean Difference [2]	-0.73, 0.61	
			p-value MMRM [2]	0.8588	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.08	
			95% CI for SMD (Hedges' g)	-1.05, 0.88	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C ability to adapt to environment by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	2.71 (0.756)	2.50 (1.000)
			LS Mean (SE) [2]	2.71 (0.321)	2.50 (0.420)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.21 (0.528)	
			95% CI for LS Mean Difference [2]	-0.98, 1.40	
			p-value MMRM [2]	0.6944	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.22	
			95% CI for SMD (Hedges' g)	-1.01, 1.45	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C ability to adapt to environment by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	9 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	3.00 (0.500)	2.25 (0.957)
			LS Mean (SE) [2]	3.00 (0.219)	2.25 (0.329)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.75 (0.395)	
			95% CI for LS Mean Difference [2]	-0.12, 1.62	
			p-value MMRM [2]	0.0841	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.02	
			95% CI for SMD (Hedges' g)	-0.24, 2.27	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.9.58 CaGI-C ability to adapt to environment by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.2370	
<10.5 years old at screening	Week 12	Absolute value	n (%)	9 (75.00)	3 (75.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
			Mean (SD)	2.56 (0.726)	2.00 (1.000)
			LS Mean (SE) [2]	2.55 (0.265)	1.98 (0.461)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.57 (0.532)	
			95% CI for LS Mean Difference [2]	-0.61, 1.75	
			p-value MMRM [2]	0.3051	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.64	
			95% CI for SMD (Hedges' g)	-0.70, 1.97	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-C ability to adapt to environment by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	2.45 (0.688)	2.75 (0.500)
			LS Mean (SE) [2]	2.45 (0.196)	2.75 (0.325)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.30 (0.379)	
			95% CI for LS Mean Difference [2]	-1.11, 0.52	
			p-value MMRM [2]	0.4496	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.41	
			95% CI for SMD (Hedges' g)	-1.57, 0.74	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-C ability to adapt to environment by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	8 (88.89)	7 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.75 (0.463)	2.57 (0.535)
			LS Mean (SE) [2]	2.75 (0.174)	2.57 (0.187)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.18 (0.256)	
			95% CI for LS Mean Difference [2]	-0.37, 0.73	
			p-value MMRM [2]	0.4918	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.33	
			95% CI for SMD (Hedges' g)	-0.69, 1.36	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-C ability to adapt to environment by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	8 (88.89)	7 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	3.00 (0.535)	2.14 (0.690)
			LS Mean (SE) [2]	2.95 (0.218)	2.14 (0.234)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.81 (0.320)	
			95% CI for LS Mean Difference [2]	0.12, 1.50	
			p-value MMRM [2]	0.0254 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.19	
			95% CI for SMD (Hedges' g)	0.07, 2.30	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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4.10.9.59 CaGI-C ability to adapt to environment by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.4705	
US	Week 12	Absolute value	n (%)	7 (87.50)	5 (83.33)
			Number of patients with missing data: n (%)	1 (12.50)	1 (16.67)
			Mean (SD)	2.57 (0.787)	2.60 (0.548)
			LS Mean (SE) [2]	2.56 (0.267)	2.58 (0.317)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.02 (0.415)	
			95% CI for LS Mean Difference [2]	-0.94, 0.91	
			p-value MMRM [2]	0.9668	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.02	
			95% CI for SMD (Hedges' g)	-1.17, 1.13	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C ability to adapt to environment by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	8 (100.00)	6 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	2.63 (0.744)	2.33 (0.816)
			LS Mean (SE) [2]	2.63 (0.274)	2.33 (0.316)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.29 (0.419)	
			95% CI for LS Mean Difference [2]	-0.62, 1.20	
			p-value MMRM [2]	0.4992	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.34	
			95% CI for SMD (Hedges' g)	-0.73, 1.41	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C ability to adapt to environment by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	10 (76.92)	5 (100.00)
			Number of patients with missing data: n (%)	3 (23.08)	0 (0.00)
			Mean (SD)	2.70 (0.483)	2.20 (0.837)
			LS Mean (SE) [2]	2.69 (0.195)	2.20 (0.274)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.49 (0.337)	
			95% CI for LS Mean Difference [2]	-0.24, 1.22	
			p-value MMRM [2]	0.1697	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.72	
			95% CI for SMD (Hedges' g)	-0.39, 1.83	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C ability to adapt to environment by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	11 (84.62)	5 (100.00)
			Number of patients with missing data: n (%)	2 (15.38)	0 (0.00)
			Mean (SD)	2.73 (0.647)	2.40 (0.548)
			LS Mean (SE) [2]	2.71 (0.188)	2.40 (0.278)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.31 (0.335)	
			95% CI for LS Mean Difference [2]	-0.41, 1.03	
			p-value MMRM [2]	0.3695	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.46	
			95% CI for SMD (Hedges' g)	-0.61, 1.53	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.9.60 CaGI-C ability to adapt to environment by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.4630	
I	Week 12	Absolute value	n (%)	8 (88.89)	4 (80.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (20.00)
			Mean (SD)	3.00 (0.000)	3.00 (0.000)
			LS Mean (SE) [2]	3.00 (0.205)	3.00 (0.296)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.00 (0.360)	
			95% CI for LS Mean Difference [2]	-0.75, 0.75	
			p-value MMRM [2]	1.0000	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.00	
			95% CI for SMD (Hedges' g)	-1.20, 1.20	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C ability to adapt to environment by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	8 (88.89)	5 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.63 (0.744)	2.40 (0.894)
			LS Mean (SE) [2]	2.63 (0.205)	2.40 (0.260)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.22 (0.331)	
			95% CI for LS Mean Difference [2]	-0.46, 0.91	
			p-value MMRM [2]	0.5040	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.37	
			95% CI for SMD (Hedges' g)	-0.76, 1.49	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C ability to adapt to environment by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	9 (75.00)	6 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			Mean (SD)	2.33 (0.707)	2.00 (0.632)
			LS Mean (SE) [2]	2.33 (0.217)	2.00 (0.262)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.33 (0.340)	
			95% CI for LS Mean Difference [2]	-0.37, 1.03	
			p-value MMRM [2]	0.3386	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.49	
			95% CI for SMD (Hedges' g)	-0.56, 1.54	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CaGI-C ability to adapt to environment by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	11 (91.67)	6 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	2.73 (0.647)	2.33 (0.516)
			LS Mean (SE) [2]	2.72 (0.194)	2.33 (0.262)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.39 (0.326)	
			95% CI for LS Mean Difference [2]	-0.28, 1.06	
			p-value MMRM [2]	0.2415	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.58	
			95% CI for SMD (Hedges' g)	-0.44, 1.60	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.9.61 CaGI-C ability to adapt to environment responders - any improvement by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Gender, p-value Chi-Square[1]	0.4048	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (14.29)
		Non-Responders [1]	8 (66.67)	3 (42.86)
		Responders	4 (33.33)	4 (57.14)
		OR (95% CI)	0.38 (0.06, 2.55)	
		RR (95% CI)	0.58 (0.21, 1.63)	
		RD % (95% CI)	-23.81 (-69.15, 21.53)	
		p-value – Fisher's Exact Test	0.3765	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	0 (0.00)
		Non-Responders [1]	7 (58.33)	3 (42.86)
		Responders	5 (41.67)	4 (57.14)
		OR (95% CI)	0.54 (0.08, 3.53)	
		RR (95% CI)	0.73 (0.29, 1.84)	
		RD % (95% CI)	-15.48 (-61.54, 30.59)	
		p-value – Fisher's Exact Test	0.6499	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CaGI-C ability to adapt to environment responders - any improvement by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (22.22)	0 (0.00)
		Non-Responders [1]	8 (88.89)	3 (75.00)
		Responders	1 (11.11)	1 (25.00)
		OR (95% CI)	0.38 (0.02, 8.10)	
		RR (95% CI)	0.44 (0.04, 5.46)	
		RD % (95% CI)	-13.89 (-61.03, 33.25)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	8 (88.89)	2 (50.00)
		Responders	1 (11.11)	2 (50.00)
		OR (95% CI)	0.13 (0.01, 2.18)	
		RR (95% CI)	0.22 (0.03, 1.80)	
		RD % (95% CI)	-38.89 (-92.02, 14.24)	
		p-value – Fisher's Exact Test	0.2028	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.9.62 CaGI-C ability to adapt to environment responders - any improvement by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Age Group, p-value Chi-Square[1]	0.0446 ***	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (25.00)	1 (25.00)
		Non-Responders [1]	9 (75.00)	2 (50.00)
		Responders	3 (25.00)	2 (50.00)
		OR (95% CI)	0.33 (0.03, 3.51)	
		RR (95% CI)	0.50 (0.13, 2.00)	
		RD % (95% CI)	-25.00 (-79.78, 29.78)	
		p-value – Fisher's Exact Test	0.5467	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [1]	7 (58.33)	3 (75.00)
		Responders	5 (41.67)	1 (25.00)
		OR (95% CI)	2.14 (0.17, 27.10)	
		RR (95% CI)	1.67 (0.27, 10.33)	
		RD % (95% CI)	16.67 (-34.11, 67.45)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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CaGI-C ability to adapt to environment responders - any improvement by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	7 (77.78)	4 (57.14)
		Responders	2 (22.22)	3 (42.86)
		OR (95% CI)	0.38 (0.04, 3.34)	
		RR (95% CI)	0.52 (0.12, 2.30)	
		RD % (95% CI)	-20.63 (-66.26, 24.99)	
		p-value – Fisher's Exact Test	0.5962	
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	8 (88.89)	2 (28.57)
		Responders	1 (11.11)	5 (71.43)
		OR (95% CI)	0.05 (0.00, 0.71)	
		RR (95% CI)	0.16 (0.02, 1.05)	
		RD % (95% CI)	-60.32 (-99.58, -21.06)	
		p-value – Fisher's Exact Test	0.0350 ***	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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4.10.9.63 CaGI-C ability to adapt to environment responders - any improvement by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Region, p-value Chi-Square[1]	0.9409	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (12.50)	1 (16.67)
		Non-Responders [1]	6 (75.00)	4 (66.67)
		Responders	2 (25.00)	2 (33.33)
		OR (95% CI)	0.67 (0.06, 6.87)	
		RR (95% CI)	0.75 (0.14, 3.90)	
		RD % (95% CI)	-8.33 (-56.53, 39.87)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	6 (75.00)	3 (50.00)
		Responders	2 (25.00)	3 (50.00)
		OR (95% CI)	0.33 (0.03, 3.20)	
		RR (95% CI)	0.50 (0.12, 2.12)	
		RD % (95% CI)	-25.00 (-75.01, 25.01)	
		p-value – Fisher's Exact Test	0.5804	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CaGI-C ability to adapt to environment responders - any improvement by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (23.08)	0 (0.00)
		Non-Responders [1]	10 (76.92)	2 (40.00)
		Responders	3 (23.08)	3 (60.00)
		OR (95% CI)	0.20 (0.02, 1.82)	
		RR (95% CI)	0.38 (0.11, 1.31)	
		RD % (95% CI)	-36.92 (-85.59, 11.74)	
		p-value – Fisher's Exact Test	0.2682	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (15.38)	0 (0.00)
		Non-Responders [1]	9 (69.23)	2 (40.00)
		Responders	4 (30.77)	3 (60.00)
		OR (95% CI)	0.30 (0.03, 2.52)	
		RR (95% CI)	0.51 (0.17, 1.52)	
		RD % (95% CI)	-29.23 (-78.96, 20.50)	
		p-value – Fisher's Exact Test	0.3260	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.9.64 CaGI-C ability to adapt to environment responders - any improvement by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.7382	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	1 (20.00)
		Non-Responders [1]	9 (100.00)	5 (100.00)
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	7 (77.78)	3 (60.00)
		Responders	2 (22.22)	2 (40.00)
		OR (95% CI)	0.43 (0.04, 4.64)	
		RR (95% CI)	0.56 (0.11, 2.83)	
		RD % (95% CI)	-17.78 (-68.59, 33.03)	
		p-value – Fisher's Exact Test	0.5804	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CaGI-C ability to adapt to environment responders - any improvement by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (25.00)	0 (0.00)
		Non-Responders [1]	7 (58.33)	1 (16.67)
		Responders	5 (41.67)	5 (83.33)
		OR (95% CI)	0.14 (0.01, 1.63)	
		RR (95% CI)	0.50 (0.23, 1.07)	
		RD % (95% CI)	-41.67 (-82.50, -0.83)	
		p-value – Fisher's Exact Test	0.1516	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	0 (0.00)
		Non-Responders [1]	8 (66.67)	2 (33.33)
		Responders	4 (33.33)	4 (66.67)
		OR (95% CI)	0.25 (0.03, 2.00)	
		RR (95% CI)	0.50 (0.19, 1.33)	
		RD % (95% CI)	-33.33 (-79.53, 12.86)	
		p-value – Fisher's Exact Test	0.3213	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.10 Subgruppenanalysen für den Endpunkt CGI-C

4.10.10.1 CGI-C ability to walk by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.0609	
Male	Week 12	Absolute value	n (%)	7 (58.33)	5 (71.43)
			Number of patients with missing data: n (%)	5 (41.67)	2 (28.57)
			Mean (SD)	2.71 (0.488)	2.80 (0.447)
			LS Mean (SE) [2]	2.71 (0.182)	2.80 (0.211)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.09 (0.278)	
			95% CI for LS Mean Difference [2]	-0.71, 0.53	
			p-value MMRM [2]	0.7470	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.17	
			95% CI for SMD (Hedges' g)	-1.32, 0.98	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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1.4.10 CGI-C
CGI-C ability to walk by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	10 (83.33)	4 (57.14)
			Number of patients with missing data: n (%)	2 (16.67)	3 (42.86)
			Mean (SD)	2.40 (0.516)	2.75 (0.500)
			LS Mean (SE) [2]	2.40 (0.162)	2.76 (0.259)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.36 (0.305)	
			95% CI for LS Mean Difference [2]	-1.03, 0.30	
			p-value MMRM [2]	0.2561	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.64	
			95% CI for SMD (Hedges' g)	-1.83, 0.55	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.
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1.4.10 CGI-C
CGI-C ability to walk by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	3.00 (0.000)	2.75 (0.500)
			LS Mean (SE) [2]	3.00 (0.106)	2.75 (0.142)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.25 (0.177)	
			95% CI for LS Mean Difference [2]	-0.15, 0.65	
			p-value MMRM [2]	0.1897	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.78	
			95% CI for SMD (Hedges' g)	-0.50, 2.06	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.
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1.4.10 CGI-C
CGI-C ability to walk by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	3.00 (0.000)	2.50 (0.577)
			LS Mean (SE) [2]	3.00 (0.112)	2.50 (0.158)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.50 (0.194)	
			95% CI for LS Mean Difference [2]	0.07, 0.93	
			p-value MMRM [2]	0.0273 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.39	
			95% CI for SMD (Hedges' g)	0.04, 2.74	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.
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4.10.10.2 CGI-C ability to walk by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.8042	
<10.5 years old at screening	Week 12	Absolute value	n (%)	7 (58.33)	3 (75.00)
			Number of patients with missing data: n (%)	5 (41.67)	1 (25.00)
			Mean (SD)	2.86 (0.378)	2.67 (0.577)
			LS Mean (SE) [2]	2.80 (0.171)	2.67 (0.257)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.14 (0.309)	
			95% CI for LS Mean Difference [2]	-0.58, 0.85	
			p-value MMRM [2]	0.6706	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.26	
			95% CI for SMD (Hedges' g)	-1.10, 1.62	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CGI-C ability to walk by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	10 (83.33)	3 (75.00)
			Number of patients with missing data: n (%)	2 (16.67)	1 (25.00)
			Mean (SD)	2.70 (0.483)	2.67 (0.577)
			LS Mean (SE) [2]	2.70 (0.159)	2.67 (0.290)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.03 (0.330)	
			95% CI for LS Mean Difference [2]	-0.69, 0.76	
			p-value MMRM [2]	0.9214	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.06	
			95% CI for SMD (Hedges' g)	-1.23, 1.35	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CGI-C ability to walk by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	7 (77.78)	6 (85.71)
			Number of patients with missing data: n (%)	2 (22.22)	1 (14.29)
			Mean (SD)	2.86 (0.378)	2.83 (0.408)
			LS Mean (SE) [2]	2.88 (0.146)	2.83 (0.159)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.04 (0.216)	
			95% CI for LS Mean Difference [2]	-0.43, 0.52	
			p-value MMRM [2]	0.8415	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.10	
			95% CI for SMD (Hedges' g)	-0.99, 1.19	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CGI-C ability to walk by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	8 (88.89)	5 (71.43)
			Number of patients with missing data: n (%)	1 (11.11)	2 (28.57)
			Mean (SD)	2.63 (0.518)	2.60 (0.548)
			LS Mean (SE) [2]	2.63 (0.185)	2.62 (0.232)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.00 (0.297)	
			95% CI for LS Mean Difference [2]	-0.65, 0.65	
			p-value MMRM [2]	0.9945	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.00	
			95% CI for SMD (Hedges' g)	-1.11, 1.12	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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4.10.10.3 CGI-C ability to walk by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.0652	
US	Week 12	Absolute value	n (%)	5 (62.50)	4 (66.67)
			Number of patients with missing data: n (%)	3 (37.50)	2 (33.33)
			Mean (SD)	3.00 (0.000)	2.50 (0.577)
			LS Mean (SE) [2]	3.01 (0.169)	2.50 (0.187)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.51 (0.252)	
			95% CI for LS Mean Difference [2]	-0.08, 1.10	
			p-value MMRM [2]	0.0806	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.14	
			95% CI for SMD (Hedges' g)	-0.31, 2.58	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CGI-C ability to walk by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	6 (75.00)	4 (66.67)
			Number of patients with missing data: n (%)	2 (25.00)	2 (33.33)
			Mean (SD)	2.83 (0.408)	2.75 (0.500)
			LS Mean (SE) [2]	2.83 (0.182)	2.75 (0.222)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.08 (0.287)	
			95% CI for LS Mean Difference [2]	-0.58, 0.75	
			p-value MMRM [2]	0.7791	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.16	
			95% CI for SMD (Hedges' g)	-1.11, 1.43	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CGI-C ability to walk by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	9 (69.23)	5 (100.00)
			Number of patients with missing data: n (%)	4 (30.77)	0 (0.00)
			Mean (SD)	2.78 (0.441)	3.00 (0.000)
			LS Mean (SE) [2]	2.74 (0.117)	3.00 (0.162)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.26 (0.200)	
			95% CI for LS Mean Difference [2]	-0.69, 0.18	
			p-value MMRM [2]	0.2206	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.66	
			95% CI for SMD (Hedges' g)	-1.78, 0.47	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CGI-C ability to walk by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	12 (92.31)	4 (80.00)
			Number of patients with missing data: n (%)	1 (7.69)	1 (20.00)
			Mean (SD)	2.58 (0.515)	2.50 (0.577)
			LS Mean (SE) [2]	2.58 (0.151)	2.50 (0.254)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.08 (0.295)	
			95% CI for LS Mean Difference [2]	-0.54, 0.71	
			p-value MMRM [2]	0.7815	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.15	
			95% CI for SMD (Hedges' g)	-0.99, 1.28	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.10.4 CGI-C ability to walk by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.6809	
I	Week 12	Absolute value	n (%)	6 (66.67)	5 (100.00)
			Number of patients with missing data: n (%)	3 (33.33)	0 (0.00)
			Mean (SD)	3.00 (0.000)	2.80 (0.447)
			LS Mean (SE) [2]	3.01 (0.116)	2.80 (0.130)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.21 (0.175)	
			95% CI for LS Mean Difference [2]	-0.18, 0.60	
			p-value MMRM [2]	0.2534	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.65	
			95% CI for SMD (Hedges' g)	-0.58, 1.87	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CGI-C ability to walk by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	7 (77.78)	5 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	2.86 (0.378)	2.80 (0.447)
			LS Mean (SE) [2]	2.86 (0.154)	2.80 (0.182)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.06 (0.238)	
			95% CI for LS Mean Difference [2]	-0.47, 0.59	
			p-value MMRM [2]	0.8154	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.12	
			95% CI for SMD (Hedges' g)	-1.03, 1.27	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CGI-C ability to walk by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	8 (66.67)	4 (66.67)
			Number of patients with missing data: n (%)	4 (33.33)	2 (33.33)
			Mean (SD)	2.75 (0.463)	2.75 (0.500)
			LS Mean (SE) [2]	2.73 (0.171)	2.75 (0.237)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.02 (0.292)	
			95% CI for LS Mean Difference [2]	-0.67, 0.63	
			p-value MMRM [2]	0.9544	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.03	
			95% CI for SMD (Hedges' g)	-1.23, 1.17	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CGI-C ability to walk by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	11 (91.67)	3 (50.00)
			Number of patients with missing data: n (%)	1 (8.33)	3 (50.00)
			Mean (SD)	2.55 (0.522)	2.33 (0.577)
			LS Mean (SE) [2]	2.55 (0.160)	2.36 (0.312)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.19 (0.350)	
			95% CI for LS Mean Difference [2]	-0.57, 0.95	
			p-value MMRM [2]	0.5980	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.32	
			95% CI for SMD (Hedges' g)	-0.96, 1.60	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.10.5 CGI-C ability to walk responders - any improvement by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Gender, p-value Chi-Square[1]	0.9567	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	5 (41.67)	2 (28.57)
		Non-Responders [1]	10 (83.33)	6 (85.71)
		Responders	2 (16.67)	1 (14.29)
		OR (95% CI)	1.20 (0.09, 16.24)	
		RR (95% CI)	1.17 (0.13, 10.66)	
		RD % (95% CI)	2.38 (-31.03, 35.80)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	3 (42.86)
		Non-Responders [1]	6 (50.00)	6 (85.71)
		Responders	6 (50.00)	1 (14.29)
		OR (95% CI)	6.00 (0.54, 66.17)	
		RR (95% CI)	3.50 (0.52, 23.42)	
		RD % (95% CI)	35.71 (-2.66, 74.08)	
		p-value – Fisher's Exact Test	0.1733	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CGI-C ability to walk responders - any improvement by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (22.22)	0 (0.00)
		Non-Responders [1]	9 (100.00)	3 (75.00)
		Responders	0 (0.00)	1 (25.00)
		OR (95% CI)	0.12 (0.00, 3.78)	
		RR (95% CI)	0.17 (0.01, 3.40)	
		RD % (95% CI)	-25.00 (-67.38, 17.38)	
		p-value – Fisher's Exact Test	0.3077	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	9 (100.00)	2 (50.00)
		Responders	0 (0.00)	2 (50.00)
		OR (95% CI)	0.05 (0.00, 1.49)	
		RR (95% CI)	0.10 (0.01, 1.71)	
		RD % (95% CI)	-45.00 (-90.86, 0.86)	
		p-value – Fisher's Exact Test	0.0769	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.10.6 CGI-C ability to walk responders - any improvement by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Age Group, p-value Chi-Square[1]	0.8971	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	5 (41.67)	1 (25.00)
		Non-Responders [1]	11 (91.67)	3 (75.00)
		Responders	1 (8.33)	1 (25.00)
		OR (95% CI)	0.27 (0.01, 5.77)	
		RR (95% CI)	0.33 (0.03, 4.19)	
		RD % (95% CI)	-16.67 (-61.89, 28.56)	
		p-value – Fisher's Exact Test	0.4500	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (16.67)	1 (25.00)
		Non-Responders [1]	9 (75.00)	3 (75.00)
		Responders	3 (25.00)	1 (25.00)
		OR (95% CI)	1.00 (0.07, 13.64)	
		RR (95% CI)	1.00 (0.14, 7.10)	
		RD % (95% CI)	0.00 (-49.00, 49.00)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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CGI-C ability to walk responders - any improvement by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (22.22)	1 (14.29)
		Non-Responders [1]	8 (88.89)	6 (85.71)
		Responders	1 (11.11)	1 (14.29)
		OR (95% CI)	0.75 (0.04, 14.58)	
		RR (95% CI)	0.78 (0.06, 10.37)	
		RD % (95% CI)	-3.17 (-36.24, 29.89)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	2 (28.57)
		Non-Responders [1]	6 (66.67)	5 (71.43)
		Responders	3 (33.33)	2 (28.57)
		OR (95% CI)	1.25 (0.15, 10.70)	
		RR (95% CI)	1.17 (0.26, 5.19)	
		RD % (95% CI)	4.76 (-40.72, 50.24)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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4.10.10.7 CGI-C ability to walk responders - any improvement by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Region, p-value Chi-Square[1]	0.8845	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (37.50)	2 (33.33)
		Non-Responders [1]	8 (100.00)	4 (66.67)
		Responders	0 (0.00)	2 (33.33)
		OR (95% CI)	0.11 (0.00, 2.72)	
		RR (95% CI)	0.16 (0.01, 2.75)	
		RD % (95% CI)	-30.16 (-68.68, 8.36)	
		p-value – Fisher's Exact Test	0.1648	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (25.00)	2 (33.33)
		Non-Responders [1]	7 (87.50)	5 (83.33)
		Responders	1 (12.50)	1 (16.67)
		OR (95% CI)	0.71 (0.04, 14.35)	
		RR (95% CI)	0.75 (0.06, 9.72)	
		RD % (95% CI)	-4.17 (-41.78, 33.44)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CGI-C ability to walk responders - any improvement by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	4 (30.77)	0 (0.00)
		Non-Responders [1]	11 (84.62)	5 (100.00)
		Responders	2 (15.38)	0 (0.00)
		OR (95% CI)	2.39 (0.10, 58.77)	
		RR (95% CI)	2.14 (0.12, 38.24)	
		RD % (95% CI)	9.52 (-20.34, 39.38)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (7.69)	1 (20.00)
		Non-Responders [1]	8 (61.54)	3 (60.00)
		Responders	5 (38.46)	2 (40.00)
		OR (95% CI)	0.94 (0.11, 7.73)	
		RR (95% CI)	0.96 (0.27, 3.44)	
		RD % (95% CI)	-1.54 (-51.97, 48.89)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.10.8 CGI-C ability to walk responders - any improvement by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.5730	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (33.33)	0 (0.00)
		Non-Responders [1]	9 (100.00)	4 (80.00)
		Responders	0 (0.00)	1 (20.00)
		OR (95% CI)	0.16 (0.01, 4.69)	
		RR (95% CI)	0.20 (0.01, 4.17)	
		RD % (95% CI)	-20.00 (-57.19, 17.19)	
		p-value – Fisher's Exact Test	0.3571	
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (22.22)	0 (0.00)
		Non-Responders [1]	8 (88.89)	4 (80.00)
		Responders	1 (11.11)	1 (20.00)
		OR (95% CI)	0.50 (0.02, 10.25)	
		RR (95% CI)	0.56 (0.04, 7.09)	
		RD % (95% CI)	-8.89 (-49.52, 31.74)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CGI-C ability to walk responders - any improvement by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	4 (33.33)	2 (33.33)
		Non-Responders [1]	10 (83.33)	5 (83.33)
		Responders	2 (16.67)	1 (16.67)
		OR (95% CI)	1.00 (0.07, 13.87)	
		RR (95% CI)	1.00 (0.11, 8.95)	
		RD % (95% CI)	0.00 (-36.52, 36.52)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (8.33)	3 (50.00)
		Non-Responders [1]	7 (58.33)	4 (66.67)
		Responders	5 (41.67)	2 (33.33)
		OR (95% CI)	1.43 (0.18, 11.09)	
		RR (95% CI)	1.25 (0.34, 4.65)	
		RD % (95% CI)	8.33 (-38.58, 55.25)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.10.9 CGI-C dependance on assistive device by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.6955	
Male	Week 12	Absolute value	n (%)	6 (50.00)	5 (71.43)
			Number of patients with missing data: n (%)	6 (50.00)	2 (28.57)
			Mean (SD)	2.83 (0.408)	2.80 (0.447)
			LS Mean (SE) [2]	2.83 (0.205)	2.80 (0.191)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.03 (0.280)	
			95% CI for LS Mean Difference [2]	-0.60, 0.67	
			p-value MMRM [2]	0.9079	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.06	
			95% CI for SMD (Hedges' g)	-1.13, 1.25	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CGI-C dependance on assistive device by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	8 (66.67)	3 (42.86)
			Number of patients with missing data: n (%)	4 (33.33)	4 (57.14)
			Mean (SD)	2.88 (0.354)	3.00 (0.000)
			LS Mean (SE) [2]	2.88 (0.110)	3.00 (0.230)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.13 (0.255)	
			95% CI for LS Mean Difference [2]	-0.70, 0.45	
			p-value MMRM [2]	0.6358	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.33	
			95% CI for SMD (Hedges' g)	-1.66, 1.01	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CGI-C dependance on assistive device by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	3.00 (0.000)	2.75 (0.500)
			LS Mean (SE) [2]	3.00 (0.110)	2.75 (0.144)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.25 (0.182)	
			95% CI for LS Mean Difference [2]	-0.16, 0.66	
			p-value MMRM [2]	0.2023	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.74	
			95% CI for SMD (Hedges' g)	-0.53, 2.02	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CGI-C dependance on assistive device by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.88 (0.354)	3.00 (0.000)
			LS Mean (SE) [2]	2.88 (0.105)	3.00 (0.148)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.12 (0.181)	
			95% CI for LS Mean Difference [2]	-0.53, 0.28	
			p-value MMRM [2]	0.5059	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.37	
			95% CI for SMD (Hedges' g)	-1.58, 0.84	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.10.10 CGI-C dependance on assistive device by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.3687	
<10.5 years old at screening	Week 12	Absolute value	n (%)	7 (58.33)	3 (75.00)
			Number of patients with missing data: n (%)	5 (41.67)	1 (25.00)
			Mean (SD)	2.86 (0.378)	2.33 (0.577)
			LS Mean (SE) [2]	2.87 (0.172)	2.33 (0.253)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.54 (0.306)	
			95% CI for LS Mean Difference [2]	-0.17, 1.24	
			p-value MMRM [2]	0.1174	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.01	
			95% CI for SMD (Hedges' g)	-0.43, 2.45	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CGI-C dependance on assistive device by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	9 (75.00)	3 (75.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
			Mean (SD)	2.78 (0.441)	3.00 (0.000)
			LS Mean (SE) [2]	2.78 (0.131)	3.00 (0.228)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.22 (0.263)	
			95% CI for LS Mean Difference [2]	-0.81, 0.36	
			p-value MMRM [2]	0.4178	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.50	
			95% CI for SMD (Hedges' g)	-1.82, 0.83	
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	6 (66.67)	6 (85.71)
			Number of patients with missing data: n (%)	3 (33.33)	1 (14.29)
			Mean (SD)	3.00 (0.000)	3.00 (0.000)
			The model did not converge		

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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CGI-C dependance on assistive device by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	7 (77.78)	4 (57.14)
			Number of patients with missing data: n (%)	2 (22.22)	3 (42.86)
			Mean (SD)	3.00 (0.000)	3.00 (0.000)
			The model did not converge		

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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4.10.10.11 CGI-C dependance on assistive device by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.3658	
US	Week 12	Absolute value	n (%)	5 (62.50)	4 (66.67)
			Number of patients with missing data: n (%)	3 (37.50)	2 (33.33)
			Mean (SD)	3.00 (0.000)	2.75 (0.500)
			LS Mean (SE) [2]	3.00 (0.102)	2.75 (0.112)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.25 (0.151)	
			95% CI for LS Mean Difference [2]	-0.07, 0.57	
			p-value MMRM [2]	0.1194	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.02	
			95% CI for SMD (Hedges' g)	-0.40, 2.43	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CGI-C dependance on assistive device by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	6 (75.00)	4 (66.67)
			Number of patients with missing data: n (%)	2 (25.00)	2 (33.33)
			Mean (SD)	3.00 (0.000)	3.00 (0.000)
			LS Mean (SE) [2]	3.00 (0.091)	3.00 (0.112)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.00 (0.144)	
			95% CI for LS Mean Difference [2]	-0.31, 0.31	
			p-value MMRM [2]	1.0000	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.00	
			95% CI for SMD (Hedges' g)	-1.27, 1.27	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CGI-C dependance on assistive device by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	8 (61.54)	5 (100.00)
			Number of patients with missing data: n (%)	5 (38.46)	0 (0.00)
			Mean (SD)	2.88 (0.354)	2.80 (0.447)
			LS Mean (SE) [2]	2.88 (0.140)	2.80 (0.173)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.08 (0.222)	
			95% CI for LS Mean Difference [2]	-0.38, 0.54	
			p-value MMRM [2]	0.7101	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.20	
			95% CI for SMD (Hedges' g)	-0.92, 1.32	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CGI-C dependance on assistive device by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	10 (76.92)	3 (60.00)
			Number of patients with missing data: n (%)	3 (23.08)	2 (40.00)
			Mean (SD)	2.80 (0.422)	3.00 (0.000)
			LS Mean (SE) [2]	2.80 (0.122)	2.98 (0.234)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.18 (0.264)	
			95% CI for LS Mean Difference [2]	-0.73, 0.36	
			p-value MMRM [2]	0.4916	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.45	
			95% CI for SMD (Hedges' g)	-1.75, 0.86	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.10.12 CGI-C dependance on assistive device by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.2781	
I	Week 12	Absolute value	n (%)	6 (66.67)	5 (100.00)
			Number of patients with missing data: n (%)	3 (33.33)	0 (0.00)
			Mean (SD)	3.00 (0.000)	3.00 (0.000)
			The model did not converge		
	Week 24	Absolute value	n (%)	7 (77.78)	5 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	3.00 (0.000)	3.00 (0.000)
			The model did not converge		

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CGI-C dependance on assistive device by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	7 (58.33)	4 (66.67)
			Number of patients with missing data: n (%)	5 (41.67)	2 (33.33)
			Mean (SD)	2.86 (0.378)	2.50 (0.577)
			LS Mean (SE) [2]	2.88 (0.175)	2.50 (0.221)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.38 (0.282)	
			95% CI for LS Mean Difference [2]	-0.21, 0.98	
			p-value MMRM [2]	0.1931	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.78	
			95% CI for SMD (Hedges' g)	-0.50, 2.06	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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CGI-C dependance on assistive device by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	9 (75.00)	2 (33.33)
			Number of patients with missing data: n (%)	3 (25.00)	4 (66.67)
			Mean (SD)	2.78 (0.441)	3.00 (0.000)
			LS Mean (SE) [2]	2.78 (0.147)	2.84 (0.345)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.06 (0.375)	
			95% CI for LS Mean Difference [2]	-0.85, 0.73	
			p-value MMRM [2]	0.8712	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.13	
			95% CI for SMD (Hedges' g)	-1.66, 1.41	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects. Default covariance structure type=unstructured.

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4.10.10.13 CGI-C dependance on assistive device responders - any improvement by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Gender, p-value Chi-Square[1]	0.9993	
Male	Week 12	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	6 (50.00)	2 (28.57)
		Non-Responders [1]	11 (91.67)	6 (85.71)
		Responders	1 (8.33)	1 (14.29)
		OR (95% CI)	0.55 (0.03, 10.37)	
		RR (95% CI)	0.58 (0.04, 7.94)	
		RD % (95% CI)	-5.95 (-36.23, 24.32)	
		p-value – Fisher's Exact Test	1.0000	
	Week 24	n (%)	12 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	4 (33.33)	4 (57.14)
		Non-Responders [1]	11 (91.67)	7 (100.00)
		Responders	1 (8.33)	0 (0.00)
		OR (95% CI)	1.96 (0.07, 54.67)	
		RR (95% CI)	1.85 (0.09, 40.05)	
		RD % (95% CI)	5.29 (-18.86, 29.43)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CGI-C dependance on assistive device responders - any improvement by gender

Gender	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (22.22)	0 (0.00)
		Non-Responders [1]	9 (100.00)	3 (75.00)
		Responders	0 (0.00)	1 (25.00)
		OR (95% CI)	0.12 (0.00, 3.78)	
		RR (95% CI)	0.17 (0.01, 3.40)	
		RD % (95% CI)	-25.00 (-67.38, 17.38)	
		p-value – Fisher's Exact Test	0.3077	
	Week 24	n (%)	9 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	8 (88.89)	4 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	1.59 (0.05, 47.52)	
		RR (95% CI)	1.50 (0.07, 30.59)	
		RD % (95% CI)	5.00 (-29.37, 39.37)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.10.14 CGI-C dependance on assistive device responders - any improvement by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Age Group, p-value Chi-Square[1]	0.9792	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	5 (41.67)	1 (25.00)
		Non-Responders [1]	11 (91.67)	2 (50.00)
		Responders	1 (8.33)	2 (50.00)
		OR (95% CI)	0.09 (0.01, 1.55)	
		RR (95% CI)	0.17 (0.02, 1.38)	
		RD % (95% CI)	-41.67 (-93.10, 9.77)	
		p-value – Fisher's Exact Test	0.1357	
	Week 24	n (%)	12 (100.00)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (25.00)	1 (25.00)
		Non-Responders [1]	10 (83.33)	4 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	2.14 (0.08, 54.22)	
		RR (95% CI)	1.92 (0.11, 33.44)	
		RD % (95% CI)	9.23 (-24.69, 43.15)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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CGI-C dependance on assistive device responders - any improvement by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (33.33)	1 (14.29)
		Non-Responders [1]	9 (100.00)	7 (100.00)
	Week 24	n (%)	9 (100.00)	7 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (22.22)	3 (42.86)
		Non-Responders [1]	9 (100.00)	7 (100.00)

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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4.10.10.15 CGI-C dependance on assistive device responders - any improvement by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*Region, p-value Chi-Square[1]	0.9791	
US	Week 12	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (37.50)	2 (33.33)
		Non-Responders [1]	8 (100.00)	5 (83.33)
		Responders	0 (0.00)	1 (16.67)
		OR (95% CI)	0.22 (0.01, 6.31)	
		RR (95% CI)	0.26 (0.01, 5.44)	
		RD % (95% CI)	-15.87 (-49.75, 18.01)	
		p-value – Fisher's Exact Test	0.4286	
	Week 24	n (%)	8 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (25.00)	2 (33.33)
		Non-Responders [1]	8 (100.00)	6 (100.00)

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CGI-C dependance on assistive device responders - any improvement by region

Region	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	5 (38.46)	0 (0.00)
		Non-Responders [1]	12 (92.31)	4 (80.00)
		Responders	1 (7.69)	1 (20.00)
		OR (95% CI)	0.33 (0.02, 6.65)	
		RR (95% CI)	0.38 (0.03, 5.04)	
		RD % (95% CI)	-12.31 (-50.24, 25.63)	
		p-value – Fisher's Exact Test	0.4902	
	Week 24	n (%)	13 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (23.08)	2 (40.00)
		Non-Responders [1]	11 (84.62)	5 (100.00)
		Responders	2 (15.38)	0 (0.00)
		OR (95% CI)	2.39 (0.10, 58.77)	
		RR (95% CI)	2.14 (0.12, 38.24)	
		RD % (95% CI)	9.52 (-20.34, 39.38)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.10.16 CGI-C dependance on assistive device responders - any improvement by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.9786	
I	Week 12	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (33.33)	0 (0.00)
		Non-Responders [1]	9 (100.00)	5 (100.00)
	Week 24	n (%)	9 (100.00)	5 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	2 (22.22)	0 (0.00)
		Non-Responders [1]	9 (100.00)	5 (100.00)
≥ II	Week 12	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	5 (41.67)	2 (33.33)
		Non-Responders [1]	11 (91.67)	4 (66.67)
		Responders	1 (8.33)	2 (33.33)
		OR (95% CI)	0.18 (0.01, 2.60)	
		RR (95% CI)	0.25 (0.03, 2.24)	
		RD % (95% CI)	-25.00 (-65.83, 15.83)	
		p-value – Fisher's Exact Test	0.2451	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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CGI-C dependance on assistive device responders - any improvement by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	n (%)	12 (100.00)	6 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders : n (%)	3 (25.00)	4 (66.67)
		Non-Responders [1]	10 (83.33)	6 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	3.10 (0.13, 75.18)	
		RR (95% CI)	2.69 (0.15, 48.64)	
		RD % (95% CI)	12.09 (-16.60, 40.78)	
		p-value – Fisher's Exact Test	0.5294	

Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: The option 'Answer not selected' has been imputed as missing value.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.11 Subgruppenanalysen für den Endpunkt CaGI-S

4.10.11.1 CaGI-S ability to walk by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.9321	
Male	Baseline	Absolute value	n (%)	11 (91.67)	5 (71.43)
			Number of patients with missing data: n (%)	1 (8.33)	2 (28.57)
			Mean (SD)	2.27 (1.348)	3.60 (0.894)
	Week 12	Absolute value	n (%)	8 (66.67)	3 (42.86)
			Number of patients with missing data: n (%)	4 (33.33)	4 (57.14)
			Mean (SD)	1.75 (0.886)	3.00 (1.000)
		Change from Baseline	n (%)	7 (58.33)	3 (42.86)
			Number of patients with missing data: n (%)	5 (41.67)	4 (57.14)
			LS Mean Change from Baseline (SE) [2]	-0.87 (0.271)	-0.41 (0.414)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.47 (0.517)	
			95% CI for LS Mean Difference [2]	-1.61, 0.67	
			p-value MMRM [2]	0.3846	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.57	
			95% CI for SMD (Hedges' g)	-1.95, 0.81	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S ability to walk by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	8 (66.67)	5 (71.43)
			Number of patients with missing data: n (%)	4 (33.33)	2 (28.57)
			Mean (SD)	2.13 (0.991)	3.60 (0.548)
		Change from Baseline	n (%)	7 (58.33)	4 (57.14)
			Number of patients with missing data: n (%)	5 (41.67)	3 (42.86)
			LS Mean Change from Baseline (SE) [2]	-0.69 (0.234)	0.26 (0.340)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.94 (0.435)	
			95% CI for LS Mean Difference [2]	-1.93, 0.05	
			p-value MMRM [2]	0.0594	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-1.27	
			95% CI for SMD (Hedges' g)	-2.63, 0.09	
Female	Baseline	Absolute value	n (%)	7 (77.78)	3 (75.00)
			Number of patients with missing data: n (%)	2 (22.22)	1 (25.00)
			Mean (SD)	2.29 (1.254)	1.67 (0.577)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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1.4.11 CaGI-S
CaGI-S ability to walk by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	2.43 (1.512)	2.25 (0.957)
		Change from Baseline	n (%)	7 (77.78)	3 (75.00)
			Number of patients with missing data: n (%)	2 (22.22)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	0.15 (0.264)	0.33 (0.408)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.18 (0.492)	
			95% CI for LS Mean Difference [2]	-1.33, 0.97	
			p-value MMRM [2]	0.7256	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.21	
			95% CI for SMD (Hedges' g)	-1.57, 1.14	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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1.4.11 CaGI-S
CaGI-S ability to walk by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.25 (1.581)	2.00 (0.816)
		Change from Baseline	n (%)	7 (77.78)	3 (75.00)
			Number of patients with missing data: n (%)	2 (22.22)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	-0.43 (0.220)	0.33 (0.341)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.75 (0.412)	
			95% CI for LS Mean Difference [2]	-1.72, 0.22	
			p-value MMRM [2]	0.1102	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-1.07	
			95% CI for SMD (Hedges' g)	-2.52, 0.38	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.11.2 CaGI-S ability to walk by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.5794	
<10.5 years old at screening	Baseline	Absolute value	n (%)	11 (91.67)	2 (50.00)
			Number of patients with missing data: n (%)	1 (8.33)	2 (50.00)
			Mean (SD)	1.91 (1.136)	2.50 (0.707)
	Week 12	Absolute value	n (%)	8 (66.67)	2 (50.00)
			Number of patients with missing data: n (%)	4 (33.33)	2 (50.00)
			Mean (SD)	1.88 (1.126)	2.50 (0.707)
		Change from Baseline	n (%)	8 (66.67)	2 (50.00)
			Number of patients with missing data: n (%)	4 (33.33)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.08 (0.260)	0.25 (0.543)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.32 (0.603)	
			95% CI for LS Mean Difference [2]	-1.75, 1.10	
			p-value MMRM [2]	0.6079	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.36	
			95% CI for SMD (Hedges' g)	-1.92, 1.20	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-S ability to walk by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	9 (75.00)	3 (75.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
			Mean (SD)	1.67 (0.866)	3.33 (0.577)
		Change from Baseline	n (%)	9 (75.00)	2 (50.00)
			Number of patients with missing data: n (%)	3 (25.00)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.33 (0.208)	0.75 (0.453)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.08 (0.498)	
			95% CI for LS Mean Difference [2]	-2.23, 0.07	
			p-value MMRM [2]	0.0618	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-1.47	
			95% CI for SMD (Hedges' g)	-3.14, 0.21	
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	7 (77.78)	6 (85.71)
			Number of patients with missing data: n (%)	2 (22.22)	1 (14.29)
			Mean (SD)	2.86 (1.345)	3.00 (1.414)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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CaGI-S ability to walk by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	7 (77.78)	5 (71.43)
			Number of patients with missing data: n (%)	2 (22.22)	2 (28.57)
			Mean (SD)	2.29 (1.380)	2.60 (1.140)
		Change from Baseline	n (%)	6 (66.67)	4 (57.14)
			Number of patients with missing data: n (%)	3 (33.33)	3 (42.86)
			LS Mean Change from Baseline (SE) [2]	-0.53 (0.414)	-0.45 (0.503)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.08 (0.651)	
			95% CI for LS Mean Difference [2]	-1.57, 1.41	
			p-value MMRM [2]	0.9010	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.07	
			95% CI for SMD (Hedges' g)	-1.34, 1.19	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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CaGI-S ability to walk by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	7 (77.78)	6 (85.71)
			Number of patients with missing data: n (%)	2 (22.22)	1 (14.29)
			Mean (SD)	2.86 (1.464)	2.67 (1.211)
		Change from Baseline	n (%)	5 (55.56)	5 (71.43)
			Number of patients with missing data: n (%)	4 (44.44)	2 (28.57)
			LS Mean Change from Baseline (SE) [2]	-0.63 (0.276)	-0.19 (0.278)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.44 (0.392)	
			95% CI for LS Mean Difference [2]	-1.36, 0.47	
			p-value MMRM [2]	0.2912	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.60	
			95% CI for SMD (Hedges' g)	-1.88, 0.67	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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4.10.11.3 CaGI-S ability to walk by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.7950	
US	Baseline	Absolute value	n (%)	6 (75.00)	4 (66.67)
			Number of patients with missing data: n (%)	2 (25.00)	2 (33.33)
			Mean (SD)	1.83 (1.602)	3.00 (1.633)
	Week 12	Absolute value	n (%)	7 (87.50)	3 (50.00)
			Number of patients with missing data: n (%)	1 (12.50)	3 (50.00)
			Mean (SD)	1.57 (0.787)	2.33 (0.577)
		Change from Baseline	n (%)	6 (75.00)	3 (50.00)
			Number of patients with missing data: n (%)	2 (25.00)	3 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.55 (0.150)	-0.34 (0.214)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.20 (0.264)	
			95% CI for LS Mean Difference [2]	-0.84, 0.43	
			p-value MMRM [2]	0.4724	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.44	
			95% CI for SMD (Hedges' g)	-1.85, 0.96	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S ability to walk by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	7 (87.50)	5 (83.33)
			Number of patients with missing data: n (%)	1 (12.50)	1 (16.67)
			Mean (SD)	1.71 (0.951)	3.00 (1.225)
		Change from Baseline	n (%)	6 (75.00)	4 (66.67)
			Number of patients with missing data: n (%)	2 (25.00)	2 (33.33)
			LS Mean Change from Baseline (SE) [2]	-0.55 (0.143)	0.11 (0.177)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.66 (0.231)	
			95% CI for LS Mean Difference [2]	-1.20, -0.12	
			p-value MMRM [2]	0.0234 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-1.56	
			95% CI for SMD (Hedges' g)	-3.03, -0.08	
Non-US	Baseline	Absolute value	n (%)	12 (92.31)	4 (80.00)
			Number of patients with missing data: n (%)	1 (7.69)	1 (20.00)
			Mean (SD)	2.50 (1.087)	2.75 (0.957)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S ability to walk by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	8 (61.54)	4 (80.00)
			Number of patients with missing data: n (%)	5 (38.46)	1 (20.00)
			Mean (SD)	2.50 (1.414)	2.75 (1.258)
		Change from Baseline	n (%)	8 (61.54)	3 (60.00)
			Number of patients with missing data: n (%)	5 (38.46)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-0.13 (0.325)	0.01 (0.538)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.14 (0.628)	
			95% CI for LS Mean Difference [2]	-1.61, 1.34	
			p-value MMRM [2]	0.8324	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.13	
			95% CI for SMD (Hedges' g)	-1.45, 1.20	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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CaGI-S ability to walk by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	9 (69.23)	4 (80.00)
			Number of patients with missing data: n (%)	4 (30.77)	1 (20.00)
			Mean (SD)	2.56 (1.424)	2.75 (0.957)
		Change from Baseline	n (%)	8 (61.54)	3 (60.00)
			Number of patients with missing data: n (%)	5 (38.46)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-0.55 (0.296)	0.34 (0.489)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.89 (0.571)	
			95% CI for LS Mean Difference [2]	-2.21, 0.43	
			p-value MMRM [2]	0.1575	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.91	
			95% CI for SMD (Hedges' g)	-2.30, 0.48	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.11.4 CaGI-S ability to walk by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.9298	
I	Baseline	Absolute value	n (%)	8 (88.89)	3 (60.00)
			Number of patients with missing data: n (%)	1 (11.11)	2 (40.00)
			Mean (SD)	1.63 (1.061)	2.00 (1.000)
	Week 12	Absolute value	n (%)	8 (88.89)	3 (60.00)
			Number of patients with missing data: n (%)	1 (11.11)	2 (40.00)
			Mean (SD)	1.63 (1.061)	2.00 (1.000)
		Change from Baseline	n (%)	7 (77.78)	2 (40.00)
			Number of patients with missing data: n (%)	2 (22.22)	3 (60.00)
			LS Mean Change from Baseline (SE) [2]	-0.14 (0.238)	-0.17 (0.463)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.02 (0.520)	
			95% CI for LS Mean Difference [2]	-1.20, 1.25	
			p-value MMRM [2]	0.9661	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.03	
			95% CI for SMD (Hedges' g)	-1.54, 1.60	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S ability to walk by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	7 (77.78)	5 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	1.57 (0.976)	2.40 (1.140)
		Change from Baseline	n (%)	6 (66.67)	3 (60.00)
			Number of patients with missing data: n (%)	3 (33.33)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-0.32 (0.125)	0.07 (0.176)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.40 (0.217)	
			95% CI for LS Mean Difference [2]	-0.92, 0.12	
			p-value MMRM [2]	0.1133	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-1.06	
			95% CI for SMD (Hedges' g)	-2.55, 0.43	
≥ II	Baseline	Absolute value	n (%)	10 (83.33)	5 (83.33)
			Number of patients with missing data: n (%)	2 (16.67)	1 (16.67)
			Mean (SD)	2.80 (1.229)	3.40 (1.140)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S ability to walk by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	7 (58.33)	4 (66.67)
			Number of patients with missing data: n (%)	5 (41.67)	2 (33.33)
			Mean (SD)	2.57 (1.272)	3.00 (0.816)
		Change from Baseline	n (%)	7 (58.33)	4 (66.67)
			Number of patients with missing data: n (%)	5 (41.67)	2 (33.33)
			LS Mean Change from Baseline (SE) [2]	-0.44 (0.360)	-0.26 (0.497)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.19 (0.619)	
			95% CI for LS Mean Difference [2]	-1.58, 1.21	
			p-value MMRM [2]	0.7689	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.17	
			95% CI for SMD (Hedges' g)	-1.40, 1.06	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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CaGI-S ability to walk by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	9 (75.00)	4 (66.67)
			Number of patients with missing data: n (%)	3 (25.00)	2 (33.33)
			Mean (SD)	2.67 (1.323)	3.50 (0.577)
		Change from Baseline	n (%)	8 (66.67)	4 (66.67)
			Number of patients with missing data: n (%)	4 (33.33)	2 (33.33)
			LS Mean Change from Baseline (SE) [2]	-0.59 (0.264)	0.24 (0.381)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.83 (0.470)	
			95% CI for LS Mean Difference [2]	-1.90, 0.23	
			p-value MMRM [2]	0.1102	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.96	
			95% CI for SMD (Hedges' g)	-2.23, 0.31	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.11.5 CaGI-S dependance on assistive device by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.1893	
Male	Baseline	Absolute value	n (%)	11 (91.67)	5 (71.43)
			Number of patients with missing data: n (%)	1 (8.33)	2 (28.57)
			Mean (SD)	2.00 (1.612)	3.40 (1.673)
	Week 12	Absolute value	n (%)	8 (66.67)	3 (42.86)
			Number of patients with missing data: n (%)	4 (33.33)	4 (57.14)
			Mean (SD)	1.63 (0.744)	3.00 (1.000)
		Change from Baseline	n (%)	7 (58.33)	3 (42.86)
			Number of patients with missing data: n (%)	5 (41.67)	4 (57.14)
			LS Mean Change from Baseline (SE) [2]	-0.85 (0.251)	-0.38 (0.413)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.47 (0.512)	
			95% CI for LS Mean Difference [2]	-1.64, 0.70	
			p-value MMRM [2]	0.3866	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.59	
			95% CI for SMD (Hedges' g)	-1.97, 0.80	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S dependance on assistive device by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	8 (66.67)	5 (71.43)
			Number of patients with missing data: n (%)	4 (33.33)	2 (28.57)
			Mean (SD)	2.00 (1.069)	2.80 (1.483)
		Change from Baseline	n (%)	7 (58.33)	4 (57.14)
			Number of patients with missing data: n (%)	5 (41.67)	3 (42.86)
			LS Mean Change from Baseline (SE) [2]	-0.52 (0.392)	-0.31 (0.514)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.20 (0.652)	
			95% CI for LS Mean Difference [2]	-1.68, 1.27	
			p-value MMRM [2]	0.7607	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.17	
			95% CI for SMD (Hedges' g)	-1.40, 1.06	
Female	Baseline	Absolute value	n (%)	6 (66.67)	2 (50.00)
			Number of patients with missing data: n (%)	3 (33.33)	2 (50.00)
			Mean (SD)	2.00 (1.265)	2.00 (0.000)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S dependance on assistive device by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	2.00 (1.414)	1.50 (1.000)
		Change from Baseline	n (%)	6 (66.67)	2 (50.00)
			Number of patients with missing data: n (%)	3 (33.33)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	0.17 (0.292)	0.00 (0.505)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.17 (0.583)	
			95% CI for LS Mean Difference [2]	-1.29, 1.62	
			p-value MMRM [2]	0.7854	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.18	
			95% CI for SMD (Hedges' g)	-1.42, 1.79	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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CaGI-S dependance on assistive device by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.13 (1.642)	2.50 (1.915)
		Change from Baseline	n (%)	6 (66.67)	2 (50.00)
			Number of patients with missing data: n (%)	3 (33.33)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.17 (0.379)	2.00 (0.657)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-2.17 (0.758)	
			95% CI for LS Mean Difference [2]	-4.04, -0.29	
			p-value MMRM [2]	0.0304 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-1.85	
			95% CI for SMD (Hedges' g)	-3.76, 0.06	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.11.6 CaGI-S dependance on assistive device by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.2393	
<10.5 years old at screening	Baseline	Absolute value	n (%)	10 (83.33)	2 (50.00)
			Number of patients with missing data: n (%)	2 (16.67)	2 (50.00)
			Mean (SD)	2.10 (1.449)	2.50 (0.707)
	Week 12	Absolute value	n (%)	8 (66.67)	2 (50.00)
			Number of patients with missing data: n (%)	4 (33.33)	2 (50.00)
			Mean (SD)	1.63 (1.061)	2.50 (0.707)
		Change from Baseline	n (%)	7 (58.33)	2 (50.00)
			Number of patients with missing data: n (%)	5 (41.67)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.30 (0.351)	0.10 (0.668)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.40 (0.754)	
			95% CI for LS Mean Difference [2]	-2.29, 1.49	
			p-value MMRM [2]	0.6167	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.34	
			95% CI for SMD (Hedges' g)	-1.92, 1.24	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-S dependance on assistive device by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	9 (75.00)	3 (75.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
			Mean (SD)	1.67 (1.000)	3.00 (0.000)
		Change from Baseline	n (%)	8 (66.67)	2 (50.00)
			Number of patients with missing data: n (%)	4 (33.33)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.51 (0.156)	0.60 (0.313)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.10 (0.350)	
			95% CI for LS Mean Difference [2]	-1.92, -0.28	
			p-value MMRM [2]	0.0158 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-2.08	
			95% CI for SMD (Hedges' g)	-3.93, -0.22	
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	7 (77.78)	5 (71.43)
			Number of patients with missing data: n (%)	2 (22.22)	2 (28.57)
			Mean (SD)	1.86 (1.574)	3.20 (1.789)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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CaGI-S dependance on assistive device by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	7 (77.78)	5 (71.43)
			Number of patients with missing data: n (%)	2 (22.22)	2 (28.57)
			Mean (SD)	2.00 (1.155)	2.00 (1.414)
		Change from Baseline	n (%)	6 (66.67)	3 (42.86)
			Number of patients with missing data: n (%)	3 (33.33)	4 (57.14)
			LS Mean Change from Baseline (SE) [2]	-0.13 (0.365)	-0.75 (0.565)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.62 (0.721)	
			95% CI for LS Mean Difference [2]	-1.09, 2.32	
			p-value MMRM [2]	0.4192	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.55	
			95% CI for SMD (Hedges' g)	-0.86, 1.97	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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CaGI-S dependance on assistive device by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	7 (77.78)	6 (85.71)
			Number of patients with missing data: n (%)	2 (22.22)	1 (14.29)
			Mean (SD)	2.57 (1.618)	2.50 (1.975)
		Change from Baseline	n (%)	5 (55.56)	4 (57.14)
			Number of patients with missing data: n (%)	4 (44.44)	3 (42.86)
			LS Mean Change from Baseline (SE) [2]	0.00 (0.741)	0.26 (0.812)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.26 (1.108)	
			95% CI for LS Mean Difference [2]	-2.88, 2.37	
			p-value MMRM [2]	0.8230	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.13	
			95% CI for SMD (Hedges' g)	-1.45, 1.19	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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4.10.11.7 CaGI-S dependance on assistive device by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.9159	
US	Baseline	Absolute value	n (%)	5 (62.50)	3 (50.00)
			Number of patients with missing data: n (%)	3 (37.50)	3 (50.00)
			Mean (SD)	1.80 (1.789)	3.00 (2.000)
	Week 12	Absolute value	n (%)	7 (87.50)	3 (50.00)
			Number of patients with missing data: n (%)	1 (12.50)	3 (50.00)
			Mean (SD)	1.29 (0.756)	2.00 (1.000)
		Change from Baseline	n (%)	5 (62.50)	2 (33.33)
			Number of patients with missing data: n (%)	3 (37.50)	4 (66.67)
	Week 24	Absolute value	n (%)	7 (87.50)	5 (83.33)
			Number of patients with missing data: n (%)	1 (12.50)	1 (16.67)
			Mean (SD)	1.29 (0.756)	2.60 (1.673)
		Change from Baseline	n (%)	5 (62.50)	3 (50.00)
			Number of patients with missing data: n (%)	3 (37.50)	3 (50.00)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S dependance on assistive device by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Baseline	Absolute value	n (%)	12 (92.31)	4 (80.00)
			Number of patients with missing data: n (%)	1 (7.69)	1 (20.00)
			Mean (SD)	2.08 (1.379)	3.00 (1.414)
	Week 12	Absolute value	n (%)	8 (61.54)	4 (80.00)
			Number of patients with missing data: n (%)	5 (38.46)	1 (20.00)
			Mean (SD)	2.25 (1.165)	2.25 (1.500)
		Change from Baseline	n (%)	8 (61.54)	3 (60.00)
			Number of patients with missing data: n (%)	5 (38.46)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-0.18 (0.374)	-0.05 (0.602)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.13 (0.716)	
			95% CI for LS Mean Difference [2]	-1.77, 1.51	
			p-value MMRM [2]	0.8566	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.11	
			95% CI for SMD (Hedges' g)	-1.44, 1.22	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S dependance on assistive device by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	9 (69.23)	4 (80.00)
			Number of patients with missing data: n (%)	4 (30.77)	1 (20.00)
			Mean (SD)	2.67 (1.414)	2.75 (1.708)
		Change from Baseline	n (%)	8 (61.54)	3 (60.00)
			Number of patients with missing data: n (%)	5 (38.46)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-0.15 (0.471)	0.62 (0.767)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.77 (0.901)	
			95% CI for LS Mean Difference [2]	-2.83, 1.29	
			p-value MMRM [2]	0.4166	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.50	
			95% CI for SMD (Hedges' g)	-1.84, 0.85	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.11.8 CaGI-S dependance on assistive device by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.7329	
I	Baseline	Absolute value	n (%)	8 (88.89)	2 (40.00)
			Number of patients with missing data: n (%)	1 (11.11)	3 (60.00)
			Mean (SD)	1.38 (1.061)	1.50 (0.707)
	Week 12	Absolute value	n (%)	8 (88.89)	3 (60.00)
			Number of patients with missing data: n (%)	1 (11.11)	2 (40.00)
			Mean (SD)	1.50 (1.069)	1.00 (0.000)
		Change from Baseline	n (%)	7 (77.78)	1 (20.00)
			Number of patients with missing data: n (%)	2 (22.22)	4 (80.00)
			LS Mean Change from Baseline (SE) [2]	0.14 (0.359)	-2.35 (0.734)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.49 (0.817)	
			95% CI for LS Mean Difference [2]	0.59, 4.39	
			p-value MMRM [2]	0.0166 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	2.10	
			95% CI for SMD (Hedges' g)	-0.31, 4.51	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

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CaGI-S dependance on assistive device by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	7 (77.78)	5 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	1.29 (0.756)	2.20 (1.789)
		Change from Baseline	n (%)	6 (66.67)	2 (40.00)
			Number of patients with missing data: n (%)	3 (33.33)	3 (60.00)
			LS Mean Change from Baseline (SE) [2]	-0.04 (0.365)	1.50 (0.670)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.54 (0.763)	
			95% CI for LS Mean Difference [2]	-3.40, 0.32	
			p-value MMRM [2]	0.0896	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-1.38	
			95% CI for SMD (Hedges' g)	-3.16, 0.40	
≥ II	Baseline	Absolute value	n (%)	9 (75.00)	5 (83.33)
			Number of patients with missing data: n (%)	3 (25.00)	1 (16.67)
			Mean (SD)	2.56 (1.590)	3.60 (1.342)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

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CaGI-S dependance on assistive device by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	7 (58.33)	4 (66.67)
			Number of patients with missing data: n (%)	5 (41.67)	2 (33.33)
			Mean (SD)	2.14 (1.069)	3.00 (0.816)
		Change from Baseline	n (%)	6 (50.00)	4 (66.67)
			Number of patients with missing data: n (%)	6 (50.00)	2 (33.33)
			LS Mean Change from Baseline (SE) [2]	-0.74 (0.420)	-0.35 (0.514)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.39 (0.673)	
			95% CI for LS Mean Difference [2]	-1.83, 1.05	
			p-value MMRM [2]	0.5709	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.35	
			95% CI for SMD (Hedges' g)	-1.62, 0.93	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
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CaGI-S dependance on assistive device by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	9 (75.00)	4 (66.67)
			Number of patients with missing data: n (%)	3 (25.00)	2 (33.33)
			Mean (SD)	2.67 (1.414)	3.25 (1.258)
		Change from Baseline	n (%)	7 (58.33)	4 (66.67)
			Number of patients with missing data: n (%)	5 (41.67)	2 (33.33)
			LS Mean Change from Baseline (SE) [2]	-0.53 (0.386)	-0.10 (0.514)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.43 (0.652)	
			95% CI for LS Mean Difference [2]	-1.83, 0.97	
			p-value MMRM [2]	0.5208	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.38	
			95% CI for SMD (Hedges' g)	-1.62, 0.86	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
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4.10.11.9 CaGI-S fine motor skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.7453	
Male	Baseline	Absolute value	n (%)	11 (91.67)	5 (71.43)
			Number of patients with missing data: n (%)	1 (8.33)	2 (28.57)
			Mean (SD)	2.09 (1.044)	2.60 (1.140)
	Week 12	Absolute value	n (%)	8 (66.67)	3 (42.86)
			Number of patients with missing data: n (%)	4 (33.33)	4 (57.14)
			Mean (SD)	1.38 (0.744)	2.00 (1.732)
		Change from Baseline	n (%)	7 (58.33)	3 (42.86)
			Number of patients with missing data: n (%)	5 (41.67)	4 (57.14)
			LS Mean Change from Baseline (SE) [2]	-0.67 (0.275)	-0.23 (0.419)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.45 (0.506)	
			95% CI for LS Mean Difference [2]	-1.60, 0.71	
			p-value MMRM [2]	0.4012	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.53	
			95% CI for SMD (Hedges' g)	-1.90, 0.85	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S fine motor skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	8 (66.67)	5 (71.43)
			Number of patients with missing data: n (%)	4 (33.33)	2 (28.57)
			Mean (SD)	2.00 (0.756)	2.60 (1.517)
		Change from Baseline	n (%)	7 (58.33)	4 (57.14)
			Number of patients with missing data: n (%)	5 (41.67)	3 (42.86)
			LS Mean Change from Baseline (SE) [2]	-0.17 (0.309)	-0.14 (0.415)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.03 (0.517)	
			95% CI for LS Mean Difference [2]	-1.20, 1.15	
			p-value MMRM [2]	0.9570	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.03	
			95% CI for SMD (Hedges' g)	-1.26, 1.20	
Female	Baseline	Absolute value	n (%)	7 (77.78)	3 (75.00)
			Number of patients with missing data: n (%)	2 (22.22)	1 (25.00)
			Mean (SD)	2.14 (1.464)	2.33 (0.577)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S fine motor skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	2.14 (1.464)	1.75 (0.957)
		Change from Baseline	n (%)	7 (77.78)	3 (75.00)
			Number of patients with missing data: n (%)	2 (22.22)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	-0.03 (0.330)	-0.98 (0.502)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.95 (0.602)	
			95% CI for LS Mean Difference [2]	-0.47, 2.37	
			p-value MMRM [2]	0.1576	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.91	
			95% CI for SMD (Hedges' g)	-0.52, 2.33	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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CaGI-S fine motor skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	2.14 (1.345)	2.75 (1.708)
		Change from Baseline	n (%)	6 (66.67)	3 (75.00)
			Number of patients with missing data: n (%)	3 (33.33)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	-0.51 (0.552)	0.35 (0.776)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.86 (0.953)	
			95% CI for LS Mean Difference [2]	-3.11, 1.39	
			p-value MMRM [2]	0.3964	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.53	
			95% CI for SMD (Hedges' g)	-1.94, 0.88	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.11.10 CaGI-S fine motor skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.4270	
<10.5 years old at screening	Baseline	Absolute value	n (%)	11 (91.67)	2 (50.00)
			Number of patients with missing data: n (%)	1 (8.33)	2 (50.00)
			Mean (SD)	1.82 (0.982)	3.50 (0.707)
	Week 12	Absolute value	n (%)	8 (66.67)	2 (50.00)
			Number of patients with missing data: n (%)	4 (33.33)	2 (50.00)
			Mean (SD)	1.38 (0.744)	2.50 (2.121)
		Change from Baseline	n (%)	8 (66.67)	2 (50.00)
			Number of patients with missing data: n (%)	4 (33.33)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.44 (0.326)	-0.53 (0.741)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.08 (0.879)	
			95% CI for LS Mean Difference [2]	-1.86, 2.03	
			p-value MMRM [2]	0.9250	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.08	
			95% CI for SMD (Hedges' g)	-1.47, 1.63	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-S fine motor skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	8 (66.67)	3 (75.00)
			Number of patients with missing data: n (%)	4 (33.33)	1 (25.00)
			Mean (SD)	1.88 (0.835)	3.00 (1.732)
		Change from Baseline	n (%)	8 (66.67)	2 (50.00)
			Number of patients with missing data: n (%)	4 (33.33)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.17 (0.346)	-0.53 (0.813)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.35 (0.914)	
			95% CI for LS Mean Difference [2]	-1.74, 2.45	
			p-value MMRM [2]	0.7074	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.30	
			95% CI for SMD (Hedges' g)	-1.26, 1.86	
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	7 (77.78)	6 (85.71)
			Number of patients with missing data: n (%)	2 (22.22)	1 (14.29)
			Mean (SD)	2.57 (1.397)	2.17 (0.753)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-S fine motor skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	7 (77.78)	5 (71.43)
			Number of patients with missing data: n (%)	2 (22.22)	2 (28.57)
			Mean (SD)	2.14 (1.464)	1.60 (0.894)
		Change from Baseline	n (%)	6 (66.67)	4 (57.14)
			Number of patients with missing data: n (%)	3 (33.33)	3 (42.86)
			LS Mean Change from Baseline (SE) [2]	-0.28 (0.367)	-0.61 (0.470)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.33 (0.608)	
			95% CI for LS Mean Difference [2]	-1.07, 1.73	
			p-value MMRM [2]	0.5998	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.31	
			95% CI for SMD (Hedges' g)	-0.97, 1.58	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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CaGI-S fine motor skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	7 (77.78)	6 (85.71)
			Number of patients with missing data: n (%)	2 (22.22)	1 (14.29)
			Mean (SD)	2.29 (1.254)	2.50 (1.517)
		Change from Baseline	n (%)	5 (55.56)	5 (71.43)
			Number of patients with missing data: n (%)	4 (44.44)	2 (28.57)
			LS Mean Change from Baseline (SE) [2]	-0.53 (0.521)	0.35 (0.507)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.87 (0.733)	
			95% CI for LS Mean Difference [2]	-2.56, 0.82	
			p-value MMRM [2]	0.2673	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.65	
			95% CI for SMD (Hedges' g)	-1.92, 0.63	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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4.10.11.11 CaGI-S fine motor skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.4971	
US	Baseline	Absolute value	n (%)	6 (75.00)	4 (66.67)
			Number of patients with missing data: n (%)	2 (25.00)	2 (33.33)
			Mean (SD)	1.67 (0.816)	2.50 (1.291)
	Week 12	Absolute value	n (%)	7 (87.50)	3 (50.00)
			Number of patients with missing data: n (%)	1 (12.50)	3 (50.00)
			Mean (SD)	1.71 (0.951)	2.33 (1.528)
		Change from Baseline	n (%)	6 (75.00)	3 (50.00)
			Number of patients with missing data: n (%)	2 (25.00)	3 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.04 (0.231)	0.04 (0.335)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.08 (0.410)	
			95% CI for LS Mean Difference [2]	-1.05, 0.89	
			p-value MMRM [2]	0.8536	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.11	
			95% CI for SMD (Hedges' g)	-1.50, 1.27	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S fine motor skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	6 (75.00)	5 (83.33)
			Number of patients with missing data: n (%)	2 (25.00)	1 (16.67)
			Mean (SD)	1.67 (0.516)	2.80 (1.304)
		Change from Baseline	n (%)	5 (62.50)	4 (66.67)
			Number of patients with missing data: n (%)	3 (37.50)	2 (33.33)
			LS Mean Change from Baseline (SE) [2]	-0.22 (0.146)	0.06 (0.168)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.28 (0.228)	
			95% CI for LS Mean Difference [2]	-0.83, 0.27	
			p-value MMRM [2]	0.2606	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.69	
			95% CI for SMD (Hedges' g)	-2.05, 0.67	
Non-US	Baseline	Absolute value	n (%)	12 (92.31)	4 (80.00)
			Number of patients with missing data: n (%)	1 (7.69)	1 (20.00)
			Mean (SD)	2.33 (1.303)	2.50 (0.577)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S fine motor skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	8 (61.54)	4 (80.00)
			Number of patients with missing data: n (%)	5 (38.46)	1 (20.00)
			Mean (SD)	1.75 (1.389)	1.50 (1.000)
		Change from Baseline	n (%)	8 (61.54)	3 (60.00)
			Number of patients with missing data: n (%)	5 (38.46)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-0.54 (0.299)	-1.34 (0.484)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.80 (0.568)	
			95% CI for LS Mean Difference [2]	-0.50, 2.11	
			p-value MMRM [2]	0.1936	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.82	
			95% CI for SMD (Hedges' g)	-0.56, 2.20	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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CaGI-S fine motor skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	9 (69.23)	4 (80.00)
			Number of patients with missing data: n (%)	4 (30.77)	1 (20.00)
			Mean (SD)	2.33 (1.225)	2.50 (1.915)
		Change from Baseline	n (%)	8 (61.54)	3 (60.00)
			Number of patients with missing data: n (%)	5 (38.46)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-0.37 (0.506)	-0.01 (0.819)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.36 (0.963)	
			95% CI for LS Mean Difference [2]	-2.55, 1.84	
			p-value MMRM [2]	0.7195	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.22	
			95% CI for SMD (Hedges' g)	-1.55, 1.11	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.11.12 CaGI-S fine motor skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.0749	
I	Baseline	Absolute value	n (%)	8 (88.89)	3 (60.00)
			Number of patients with missing data: n (%)	1 (11.11)	2 (40.00)
			Mean (SD)	1.50 (0.756)	2.33 (0.577)
	Week 12	Absolute value	n (%)	8 (88.89)	3 (60.00)
			Number of patients with missing data: n (%)	1 (11.11)	2 (40.00)
			Mean (SD)	1.38 (0.518)	2.00 (1.000)
		Change from Baseline	n (%)	7 (77.78)	2 (40.00)
			Number of patients with missing data: n (%)	2 (22.22)	3 (60.00)
			LS Mean Change from Baseline (SE) [2]	-0.42 (0.196)	-0.26 (0.356)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.16 (0.409)	
			95% CI for LS Mean Difference [2]	-1.11, 0.79	
			p-value MMRM [2]	0.7027	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.26	
			95% CI for SMD (Hedges' g)	-1.84, 1.32	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S fine motor skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	6 (66.67)	5 (100.00)
			Number of patients with missing data: n (%)	3 (33.33)	0 (0.00)
			Mean (SD)	1.50 (0.548)	3.40 (1.140)
		Change from Baseline	n (%)	5 (55.56)	3 (60.00)
			Number of patients with missing data: n (%)	4 (44.44)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-0.20 (0.410)	1.39 (0.546)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.59 (0.687)	
			95% CI for LS Mean Difference [2]	-3.22, 0.03	
			p-value MMRM [2]	0.0535	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-1.42	
			95% CI for SMD (Hedges' g)	-3.06, 0.22	
≥ II	Baseline	Absolute value	n (%)	10 (83.33)	5 (83.33)
			Number of patients with missing data: n (%)	2 (16.67)	1 (16.67)
			Mean (SD)	2.60 (1.265)	2.60 (1.140)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S fine motor skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	7 (58.33)	4 (66.67)
			Number of patients with missing data: n (%)	5 (41.67)	2 (33.33)
			Mean (SD)	2.14 (1.574)	1.75 (1.500)
		Change from Baseline	n (%)	7 (58.33)	4 (66.67)
			Number of patients with missing data: n (%)	5 (41.67)	2 (33.33)
			LS Mean Change from Baseline (SE) [2]	-0.33 (0.376)	-0.76 (0.501)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.43 (0.626)	
			95% CI for LS Mean Difference [2]	-1.01, 1.86	
			p-value MMRM [2]	0.5157	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.37	
			95% CI for SMD (Hedges' g)	-0.87, 1.61	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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CaGI-S fine motor skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	9 (75.00)	4 (66.67)
			Number of patients with missing data: n (%)	3 (25.00)	2 (33.33)
			Mean (SD)	2.44 (1.130)	1.75 (1.500)
		Change from Baseline	n (%)	8 (66.67)	4 (66.67)
			Number of patients with missing data: n (%)	4 (33.33)	2 (33.33)
			LS Mean Change from Baseline (SE) [2]	-0.34 (0.327)	-0.76 (0.461)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.41 (0.565)	
			95% CI for LS Mean Difference [2]	-0.87, 1.69	
			p-value MMRM [2]	0.4855	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.38	
			95% CI for SMD (Hedges' g)	-0.83, 1.60	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.11.13 CaGI-S gross motor skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.5200	
Male	Baseline	Absolute value	n (%)	11 (91.67)	5 (71.43)
			Number of patients with missing data: n (%)	1 (8.33)	2 (28.57)
			Mean (SD)	2.18 (1.401)	4.00 (0.707)
	Week 12	Absolute value	n (%)	8 (66.67)	3 (42.86)
			Number of patients with missing data: n (%)	4 (33.33)	4 (57.14)
			Mean (SD)	2.00 (1.309)	3.67 (0.577)
		Change from Baseline	n (%)	7 (58.33)	3 (42.86)
			Number of patients with missing data: n (%)	5 (41.67)	4 (57.14)
			LS Mean Change from Baseline (SE) [2]	-0.15 (0.348)	-0.43 (0.542)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.28 (0.740)	
			95% CI for LS Mean Difference [2]	-1.37, 1.92	
			p-value MMRM [2]	0.7163	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.26	
			95% CI for SMD (Hedges' g)	-1.10, 1.62	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S gross motor skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	8 (66.67)	5 (71.43)
			Number of patients with missing data: n (%)	4 (33.33)	2 (28.57)
			Mean (SD)	2.50 (1.414)	3.80 (0.837)
		Change from Baseline	n (%)	7 (58.33)	4 (57.14)
			Number of patients with missing data: n (%)	5 (41.67)	3 (42.86)
			LS Mean Change from Baseline (SE) [2]	-0.12 (0.401)	0.06 (0.599)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.19 (0.768)	
			95% CI for LS Mean Difference [2]	-1.89, 1.52	
			p-value MMRM [2]	0.8137	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.15	
			95% CI for SMD (Hedges' g)	-1.38, 1.08	
Female	Baseline	Absolute value	n (%)	7 (77.78)	3 (75.00)
			Number of patients with missing data: n (%)	2 (22.22)	1 (25.00)
			Mean (SD)	1.86 (0.690)	2.33 (0.577)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S gross motor skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	2.00 (1.155)	2.75 (1.258)
		Change from Baseline	n (%)	7 (77.78)	3 (75.00)
			Number of patients with missing data: n (%)	2 (22.22)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	0.09 (0.441)	0.45 (0.686)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.36 (0.831)	
			95% CI for LS Mean Difference [2]	-2.28, 1.57	
			p-value MMRM [2]	0.6788	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.26	
			95% CI for SMD (Hedges' g)	-1.61, 1.10	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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CaGI-S gross motor skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.38 (1.408)	2.75 (1.500)
		Change from Baseline	n (%)	7 (77.78)	3 (75.00)
			Number of patients with missing data: n (%)	2 (22.22)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	0.09 (0.486)	0.78 (0.755)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.69 (0.912)	
			95% CI for LS Mean Difference [2]	-2.80, 1.42	
			p-value MMRM [2]	0.4707	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.45	
			95% CI for SMD (Hedges' g)	-1.82, 0.92	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.11.14 CaGI-S gross motor skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.4268	
<10.5 years old at screening	Baseline	Absolute value	n (%)	11 (91.67)	2 (50.00)
			Number of patients with missing data: n (%)	1 (8.33)	2 (50.00)
			Mean (SD)	1.91 (1.221)	3.50 (0.707)
	Week 12	Absolute value	n (%)	8 (66.67)	2 (50.00)
			Number of patients with missing data: n (%)	4 (33.33)	2 (50.00)
			Mean (SD)	1.50 (0.756)	3.50 (0.707)
		Change from Baseline	n (%)	8 (66.67)	2 (50.00)
			Number of patients with missing data: n (%)	4 (33.33)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.28 (0.154)	0.39 (0.332)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.66 (0.409)	
			95% CI for LS Mean Difference [2]	-1.58, 0.25	
			p-value MMRM [2]	0.1371	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-1.28	
			95% CI for SMD (Hedges' g)	-2.95, 0.39	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-S gross motor skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	9 (75.00)	3 (75.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
			Mean (SD)	1.78 (0.833)	3.00 (1.000)
		Change from Baseline	n (%)	9 (75.00)	2 (50.00)
			Number of patients with missing data: n (%)	3 (25.00)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.26 (0.217)	-0.11 (0.501)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.15 (0.554)	
			95% CI for LS Mean Difference [2]	-1.41, 1.12	
			p-value MMRM [2]	0.7957	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.19	
			95% CI for SMD (Hedges' g)	-1.72, 1.34	
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	7 (77.78)	6 (85.71)
			Number of patients with missing data: n (%)	2 (22.22)	1 (14.29)
			Mean (SD)	2.29 (1.113)	3.33 (1.211)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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CaGI-S gross motor skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	7 (77.78)	5 (71.43)
			Number of patients with missing data: n (%)	2 (22.22)	2 (28.57)
			Mean (SD)	2.57 (1.397)	3.00 (1.225)
		Change from Baseline	n (%)	6 (66.67)	4 (57.14)
			Number of patients with missing data: n (%)	3 (33.33)	3 (42.86)
			LS Mean Change from Baseline (SE) [2]	0.28 (0.525)	-0.07 (0.642)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.35 (0.857)	
			95% CI for LS Mean Difference [2]	-1.62, 2.32	
			p-value MMRM [2]	0.6946	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.23	
			95% CI for SMD (Hedges' g)	-1.04, 1.50	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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CaGI-S gross motor skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	7 (77.78)	6 (85.71)
			Number of patients with missing data: n (%)	2 (22.22)	1 (14.29)
			Mean (SD)	3.29 (1.496)	3.50 (1.378)
		Change from Baseline	n (%)	5 (55.56)	5 (71.43)
			Number of patients with missing data: n (%)	4 (44.44)	2 (28.57)
			LS Mean Change from Baseline (SE) [2]	0.45 (0.620)	0.65 (0.629)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.20 (0.903)	
			95% CI for LS Mean Difference [2]	-2.27, 1.87	
			p-value MMRM [2]	0.8325	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.12	
			95% CI for SMD (Hedges' g)	-1.36, 1.12	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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4.10.11.15 CaGI-S gross motor skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.5337	
US	Baseline	Absolute value	n (%)	6 (75.00)	4 (66.67)
			Number of patients with missing data: n (%)	2 (25.00)	2 (33.33)
			Mean (SD)	1.67 (1.211)	3.75 (1.258)
	Week 12	Absolute value	n (%)	7 (87.50)	3 (50.00)
			Number of patients with missing data: n (%)	1 (12.50)	3 (50.00)
			Mean (SD)	1.71 (1.113)	3.67 (0.577)
		Change from Baseline	n (%)	6 (75.00)	3 (50.00)
			Number of patients with missing data: n (%)	2 (25.00)	3 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.20 (0.490)	1.01 (0.627)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.21 (0.797)	
			95% CI for LS Mean Difference [2]	-3.16, 0.74	
			p-value MMRM [2]	0.1797	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.82	
			95% CI for SMD (Hedges' g)	-2.27, 0.63	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S gross motor skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	7 (87.50)	5 (83.33)
			Number of patients with missing data: n (%)	1 (12.50)	1 (16.67)
			Mean (SD)	1.71 (0.951)	3.40 (1.140)
		Change from Baseline	n (%)	6 (75.00)	4 (66.67)
			Number of patients with missing data: n (%)	2 (25.00)	2 (33.33)
			LS Mean Change from Baseline (SE) [2]	-0.37 (0.153)	0.10 (0.191)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.47 (0.252)	
			95% CI for LS Mean Difference [2]	-1.04, 0.10	
			p-value MMRM [2]	0.0951	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-1.07	
			95% CI for SMD (Hedges' g)	-2.44, 0.30	
Non-US	Baseline	Absolute value	n (%)	12 (92.31)	4 (80.00)
			Number of patients with missing data: n (%)	1 (7.69)	1 (20.00)
			Mean (SD)	2.25 (1.138)	3.00 (0.816)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S gross motor skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	8 (61.54)	4 (80.00)
			Number of patients with missing data: n (%)	5 (38.46)	1 (20.00)
			Mean (SD)	2.25 (1.282)	2.75 (1.258)
		Change from Baseline	n (%)	8 (61.54)	3 (60.00)
			Number of patients with missing data: n (%)	5 (38.46)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	0.17 (0.353)	-0.28 (0.552)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.45 (0.700)	
			95% CI for LS Mean Difference [2]	-1.18, 2.08	
			p-value MMRM [2]	0.5378	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.38	
			95% CI for SMD (Hedges' g)	-0.96, 1.72	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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CaGI-S gross motor skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	9 (69.23)	4 (80.00)
			Number of patients with missing data: n (%)	4 (30.77)	1 (20.00)
			Mean (SD)	3.00 (1.414)	3.25 (1.500)
		Change from Baseline	n (%)	8 (61.54)	3 (60.00)
			Number of patients with missing data: n (%)	5 (38.46)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	0.24 (0.551)	0.72 (0.915)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.48 (1.068)	
			95% CI for LS Mean Difference [2]	-3.02, 2.06	
			p-value MMRM [2]	0.6667	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.25	
			95% CI for SMD (Hedges' g)	-1.58, 1.08	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.11.16 CaGI-S gross motor skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.1003	
I	Baseline	Absolute value	n (%)	8 (88.89)	3 (60.00)
			Number of patients with missing data: n (%)	1 (11.11)	2 (40.00)
			Mean (SD)	1.38 (0.744)	2.67 (1.155)
	Week 12	Absolute value	n (%)	8 (88.89)	3 (60.00)
			Number of patients with missing data: n (%)	1 (11.11)	2 (40.00)
			Mean (SD)	1.50 (0.756)	2.67 (1.528)
		Change from Baseline	n (%)	7 (77.78)	2 (40.00)
			Number of patients with missing data: n (%)	2 (22.22)	3 (60.00)
			LS Mean Change from Baseline (SE) [2]	-0.06 (0.361)	1.21 (0.559)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.28 (0.665)	
			95% CI for LS Mean Difference [2]	-2.82, 0.26	
			p-value MMRM [2]	0.0916	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-1.16	
			95% CI for SMD (Hedges' g)	-2.84, 0.53	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S gross motor skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	7 (77.78)	5 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	1.57 (0.787)	3.00 (1.225)
		Change from Baseline	n (%)	6 (66.67)	3 (60.00)
			Number of patients with missing data: n (%)	3 (33.33)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-0.20 (0.374)	0.87 (0.571)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.07 (0.683)	
			95% CI for LS Mean Difference [2]	-2.65, 0.50	
			p-value MMRM [2]	0.1549	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.97	
			95% CI for SMD (Hedges' g)	-2.45, 0.50	
≥ II	Baseline	Absolute value	n (%)	10 (83.33)	5 (83.33)
			Number of patients with missing data: n (%)	2 (16.67)	1 (16.67)
			Mean (SD)	2.60 (1.174)	3.80 (0.837)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S gross motor skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	7 (58.33)	4 (66.67)
			Number of patients with missing data: n (%)	5 (41.67)	2 (33.33)
			Mean (SD)	2.57 (1.397)	3.50 (0.577)
		Change from Baseline	n (%)	7 (58.33)	4 (66.67)
			Number of patients with missing data: n (%)	5 (41.67)	2 (33.33)
			LS Mean Change from Baseline (SE) [2]	-0.13 (0.413)	-0.05 (0.590)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.08 (0.786)	
			95% CI for LS Mean Difference [2]	-1.80, 1.65	
			p-value MMRM [2]	0.9255	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.06	
			95% CI for SMD (Hedges' g)	-1.29, 1.17	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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CaGI-S gross motor skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	9 (75.00)	4 (66.67)
			Number of patients with missing data: n (%)	3 (25.00)	2 (33.33)
			Mean (SD)	3.11 (1.364)	3.75 (1.258)
		Change from Baseline	n (%)	8 (66.67)	4 (66.67)
			Number of patients with missing data: n (%)	4 (33.33)	2 (33.33)
			LS Mean Change from Baseline (SE) [2]	0.08 (0.410)	0.20 (0.633)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.12 (0.797)	
			95% CI for LS Mean Difference [2]	-1.90, 1.66	
			p-value MMRM [2]	0.8864	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.09	
			95% CI for SMD (Hedges' g)	-1.29, 1.12	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.11.17 CaGI-S daily living skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.9275	
Male	Baseline	Absolute value	n (%)	11 (91.67)	5 (71.43)
			Number of patients with missing data: n (%)	1 (8.33)	2 (28.57)
			Mean (SD)	1.82 (1.079)	2.80 (1.304)
	Week 12	Absolute value	n (%)	8 (66.67)	3 (42.86)
			Number of patients with missing data: n (%)	4 (33.33)	4 (57.14)
			Mean (SD)	1.50 (0.756)	2.00 (0.000)
		Change from Baseline	n (%)	7 (58.33)	3 (42.86)
			Number of patients with missing data: n (%)	5 (41.67)	4 (57.14)
			LS Mean Change from Baseline (SE) [2]	-0.09 (0.259)	-0.50 (0.408)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.41 (0.537)	
			95% CI for LS Mean Difference [2]	-0.78, 1.59	
			p-value MMRM [2]	0.4661	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.51	
			95% CI for SMD (Hedges' g)	-0.86, 1.89	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S daily living skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	8 (66.67)	5 (71.43)
			Number of patients with missing data: n (%)	4 (33.33)	2 (28.57)
			Mean (SD)	1.88 (1.126)	2.40 (1.140)
		Change from Baseline	n (%)	7 (58.33)	4 (57.14)
			Number of patients with missing data: n (%)	5 (41.67)	3 (42.86)
			LS Mean Change from Baseline (SE) [2]	0.18 (0.461)	0.24 (0.624)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.05 (0.785)	
			95% CI for LS Mean Difference [2]	-1.84, 1.74	
			p-value MMRM [2]	0.9490	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.04	
			95% CI for SMD (Hedges' g)	-1.26, 1.19	
Female	Baseline	Absolute value	n (%)	7 (77.78)	3 (75.00)
			Number of patients with missing data: n (%)	2 (22.22)	1 (25.00)
			Mean (SD)	2.43 (1.512)	3.00 (2.000)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S daily living skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	1.57 (1.512)	1.25 (0.500)
		Change from Baseline	n (%)	7 (77.78)	3 (75.00)
			Number of patients with missing data: n (%)	2 (22.22)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	-0.86 (0.514)	-1.64 (0.790)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.78 (0.943)	
			95% CI for LS Mean Difference [2]	-1.47, 3.03	
			p-value MMRM [2]	0.4370	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.47	
			95% CI for SMD (Hedges' g)	-0.90, 1.84	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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CaGI-S daily living skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	8 (88.89)	3 (75.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (25.00)
			Mean (SD)	2.25 (1.581)	1.67 (1.155)
		Change from Baseline	n (%)	7 (77.78)	2 (50.00)
			Number of patients with missing data: n (%)	2 (22.22)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.43 (0.233)	-0.41 (0.410)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.02 (0.470)	
			95% CI for LS Mean Difference [2]	-1.21, 1.16	
			p-value MMRM [2]	0.9647	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.03	
			95% CI for SMD (Hedges' g)	-1.60, 1.54	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.11.18 CaGI-S daily living skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.6494	
<10.5 years old at screening	Baseline	Absolute value	n (%)	11 (91.67)	2 (50.00)
			Number of patients with missing data: n (%)	1 (8.33)	2 (50.00)
			Mean (SD)	1.91 (1.221)	3.50 (0.707)
	Week 12	Absolute value	n (%)	8 (66.67)	2 (50.00)
			Number of patients with missing data: n (%)	4 (33.33)	2 (50.00)
			Mean (SD)	1.13 (0.354)	2.00 (0.000)
		Change from Baseline	n (%)	8 (66.67)	2 (50.00)
			Number of patients with missing data: n (%)	4 (33.33)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.96 (0.144)	0.06 (0.328)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.02 (0.385)	
			95% CI for LS Mean Difference [2]	-1.93, -0.10	
			p-value MMRM [2]	0.0336 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-2.00	
			95% CI for SMD (Hedges' g)	-3.84, -0.17	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-S daily living skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	9 (75.00)	3 (75.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
			Mean (SD)	1.78 (1.202)	2.00 (1.000)
		Change from Baseline	n (%)	9 (75.00)	2 (50.00)
			Number of patients with missing data: n (%)	3 (25.00)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.34 (0.440)	0.06 (0.949)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.40 (1.050)	
			95% CI for LS Mean Difference [2]	-2.79, 1.99	
			p-value MMRM [2]	0.7122	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.26	
			95% CI for SMD (Hedges' g)	-1.80, 1.28	
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	7 (77.78)	6 (85.71)
			Number of patients with missing data: n (%)	2 (22.22)	1 (14.29)
			Mean (SD)	2.29 (1.380)	2.67 (1.633)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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CaGI-S daily living skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	7 (77.78)	5 (71.43)
			Number of patients with missing data: n (%)	2 (22.22)	2 (28.57)
			Mean (SD)	2.00 (1.528)	1.40 (0.548)
		Change from Baseline	n (%)	6 (66.67)	4 (57.14)
			Number of patients with missing data: n (%)	3 (33.33)	3 (42.86)
			LS Mean Change from Baseline (SE) [2]	-0.18 (0.441)	-1.07 (0.539)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.88 (0.698)	
			95% CI for LS Mean Difference [2]	-0.73, 2.50	
			p-value MMRM [2]	0.2416	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.69	
			95% CI for SMD (Hedges' g)	-0.62, 2.00	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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CaGI-S daily living skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	7 (77.78)	5 (71.43)
			Number of patients with missing data: n (%)	2 (22.22)	2 (28.57)
			Mean (SD)	2.43 (1.512)	2.20 (1.304)
		Change from Baseline	n (%)	5 (55.56)	4 (57.14)
			Number of patients with missing data: n (%)	4 (44.44)	3 (42.86)
			LS Mean Change from Baseline (SE) [2]	-0.04 (0.431)	0.27 (0.491)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.31 (0.655)	
			95% CI for LS Mean Difference [2]	-2.00, 1.38	
			p-value MMRM [2]	0.6553	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.24	
			95% CI for SMD (Hedges' g)	-1.56, 1.08	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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4.10.11.19 CaGI-S daily living skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.5949	
US	Baseline	Absolute value	n (%)	6 (75.00)	4 (66.67)
			Number of patients with missing data: n (%)	2 (25.00)	2 (33.33)
			Mean (SD)	1.50 (0.837)	2.00 (1.414)
	Week 12	Absolute value	n (%)	7 (87.50)	3 (50.00)
			Number of patients with missing data: n (%)	1 (12.50)	3 (50.00)
			Mean (SD)	1.29 (0.756)	1.67 (0.577)
		Change from Baseline	n (%)	6 (75.00)	3 (50.00)
			Number of patients with missing data: n (%)	2 (25.00)	3 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.27 (0.218)	-0.35 (0.309)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.09 (0.392)	
			95% CI for LS Mean Difference [2]	-0.83, 1.01	
			p-value MMRM [2]	0.8292	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.13	
			95% CI for SMD (Hedges' g)	-1.25, 1.52	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S daily living skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	7 (87.50)	5 (83.33)
			Number of patients with missing data: n (%)	1 (12.50)	1 (16.67)
			Mean (SD)	1.14 (0.378)	2.00 (1.225)
		Change from Baseline	n (%)	6 (75.00)	4 (66.67)
			Number of patients with missing data: n (%)	2 (25.00)	2 (33.33)
			LS Mean Change from Baseline (SE) [2]	-0.43 (0.452)	0.11 (0.553)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.55 (0.718)	
			95% CI for LS Mean Difference [2]	-2.25, 1.16	
			p-value MMRM [2]	0.4734	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.40	
			95% CI for SMD (Hedges' g)	-1.69, 0.88	
Non-US	Baseline	Absolute value	n (%)	12 (92.31)	4 (80.00)
			Number of patients with missing data: n (%)	1 (7.69)	1 (20.00)
			Mean (SD)	2.33 (1.371)	3.75 (0.957)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S daily living skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	8 (61.54)	4 (80.00)
			Number of patients with missing data: n (%)	5 (38.46)	1 (20.00)
			Mean (SD)	1.75 (1.389)	1.50 (0.577)
		Change from Baseline	n (%)	8 (61.54)	3 (60.00)
			Number of patients with missing data: n (%)	5 (38.46)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-0.61 (0.406)	-1.58 (0.716)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.97 (0.839)	
			95% CI for LS Mean Difference [2]	-0.91, 2.84	
			p-value MMRM [2]	0.2758	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.72	
			95% CI for SMD (Hedges' g)	-0.64, 2.09	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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CaGI-S daily living skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	9 (69.23)	3 (60.00)
			Number of patients with missing data: n (%)	4 (30.77)	2 (40.00)
			Mean (SD)	2.78 (1.394)	2.33 (1.155)
		Change from Baseline	n (%)	8 (61.54)	2 (40.00)
			Number of patients with missing data: n (%)	5 (38.46)	3 (60.00)
			LS Mean Change from Baseline (SE) [2]	0.05 (0.317)	-0.30 (0.613)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.36 (0.697)	
			95% CI for LS Mean Difference [2]	-1.28, 1.99	
			p-value MMRM [2]	0.6240	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.33	
			95% CI for SMD (Hedges' g)	-1.23, 1.89	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.11.20 CaGI-S daily living skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.9145	
I	Baseline	Absolute value	n (%)	8 (88.89)	3 (60.00)
			Number of patients with missing data: n (%)	1 (11.11)	2 (40.00)
			Mean (SD)	1.50 (1.069)	2.33 (2.309)
	Week 12	Absolute value	n (%)	8 (88.89)	3 (60.00)
			Number of patients with missing data: n (%)	1 (11.11)	2 (40.00)
			Mean (SD)	1.13 (0.354)	1.00 (0.000)
		Change from Baseline	n (%)	7 (77.78)	2 (40.00)
			Number of patients with missing data: n (%)	2 (22.22)	3 (60.00)
			LS Mean Change from Baseline (SE) [2]	-0.54 (0.153)	-0.87 (0.326)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.33 (0.365)	
			95% CI for LS Mean Difference [2]	-0.60, 1.25	
			p-value MMRM [2]	0.4065	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.62	
			95% CI for SMD (Hedges' g)	-0.99, 2.22	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S daily living skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	7 (77.78)	4 (80.00)
			Number of patients with missing data: n (%)	2 (22.22)	1 (20.00)
			Mean (SD)	1.43 (0.787)	1.50 (0.577)
		Change from Baseline	n (%)	6 (66.67)	2 (40.00)
			Number of patients with missing data: n (%)	3 (33.33)	3 (60.00)
			LS Mean Change from Baseline (SE) [2]	-0.82 (0.674)	0.44 (1.502)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.26 (1.668)	
			95% CI for LS Mean Difference [2]	-17.33, 14.81	
			p-value MMRM [2]	0.5758	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.14	
			95% CI for SMD (Hedges' g)	-1.75, 1.46	
≥ II	Baseline	Absolute value	n (%)	10 (83.33)	5 (83.33)
			Number of patients with missing data: n (%)	2 (16.67)	1 (16.67)
			Mean (SD)	2.50 (1.269)	3.20 (0.837)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S daily living skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	7 (58.33)	4 (66.67)
			Number of patients with missing data: n (%)	5 (41.67)	2 (33.33)
			Mean (SD)	2.00 (1.528)	2.00 (0.000)
		Change from Baseline	n (%)	7 (58.33)	4 (66.67)
			Number of patients with missing data: n (%)	5 (41.67)	2 (33.33)
			LS Mean Change from Baseline (SE) [2]	-0.28 (0.286)	-0.99 (0.396)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.71 (0.496)	
			95% CI for LS Mean Difference [2]	-0.42, 1.83	
			p-value MMRM [2]	0.1888	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.80	
			95% CI for SMD (Hedges' g)	-0.49, 2.08	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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CaGI-S daily living skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	9 (75.00)	4 (66.67)
			Number of patients with missing data: n (%)	3 (25.00)	2 (33.33)
			Mean (SD)	2.56 (1.509)	2.75 (1.258)
		Change from Baseline	n (%)	8 (66.67)	4 (66.67)
			Number of patients with missing data: n (%)	4 (33.33)	2 (33.33)
			LS Mean Change from Baseline (SE) [2]	-0.13 (0.498)	-0.24 (0.708)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.11 (0.868)	
			95% CI for LS Mean Difference [2]	-1.85, 2.08	
			p-value MMRM [2]	0.9000	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.07	
			95% CI for SMD (Hedges' g)	-1.13, 1.27	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.11.21 CaGI-S communication skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.2819	
Male	Baseline	Absolute value	n (%)	11 (91.67)	5 (71.43)
			Number of patients with missing data: n (%)	1 (8.33)	2 (28.57)
			Mean (SD)	2.00 (1.095)	2.60 (1.517)
	Week 12	Absolute value	n (%)	8 (66.67)	3 (42.86)
			Number of patients with missing data: n (%)	4 (33.33)	4 (57.14)
			Mean (SD)	1.25 (0.463)	2.33 (2.309)
		Change from Baseline	n (%)	7 (58.33)	3 (42.86)
			Number of patients with missing data: n (%)	5 (41.67)	4 (57.14)
			LS Mean Change from Baseline (SE) [2]	-0.56 (0.203)	-0.35 (0.303)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.20 (0.372)	
			95% CI for LS Mean Difference [2]	-1.04, 0.64	
			p-value MMRM [2]	0.5979	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.33	
			95% CI for SMD (Hedges' g)	-1.69, 1.04	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S communication skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	8 (66.67)	5 (71.43)
			Number of patients with missing data: n (%)	4 (33.33)	2 (28.57)
			Mean (SD)	2.13 (0.835)	2.00 (1.732)
		Change from Baseline	n (%)	7 (58.33)	4 (57.14)
			Number of patients with missing data: n (%)	5 (41.67)	3 (42.86)
			LS Mean Change from Baseline (SE) [2]	-0.10 (0.234)	-0.43 (0.320)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.33 (0.398)	
			95% CI for LS Mean Difference [2]	-0.57, 1.23	
			p-value MMRM [2]	0.4285	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.46	
			95% CI for SMD (Hedges' g)	-0.79, 1.71	
Female	Baseline	Absolute value	n (%)	7 (77.78)	3 (75.00)
			Number of patients with missing data: n (%)	2 (22.22)	1 (25.00)
			Mean (SD)	2.00 (1.732)	3.67 (2.309)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S communication skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	2.14 (1.345)	2.25 (0.957)
		Change from Baseline	n (%)	7 (77.78)	3 (75.00)
			Number of patients with missing data: n (%)	2 (22.22)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	-0.02 (0.386)	-1.09 (0.637)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.07 (0.771)	
			95% CI for LS Mean Difference [2]	-0.74, 2.88	
			p-value MMRM [2]	0.2058	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.85	
			95% CI for SMD (Hedges' g)	-0.56, 2.27	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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CaGI-S communication skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	8 (88.89)	3 (75.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (25.00)
			Mean (SD)	2.13 (1.553)	2.67 (0.577)
		Change from Baseline	n (%)	7 (77.78)	2 (50.00)
			Number of patients with missing data: n (%)	2 (22.22)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.31 (0.336)	-0.88 (0.588)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.57 (0.699)	
			95% CI for LS Mean Difference [2]	-1.36, 2.51	
			p-value MMRM [2]	0.4581	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.46	
			95% CI for SMD (Hedges' g)	-1.13, 2.05	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.11.22 CaGI-S communication skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.1847	
<10.5 years old at screening	Baseline	Absolute value	n (%)	11 (91.67)	2 (50.00)
			Number of patients with missing data: n (%)	1 (8.33)	2 (50.00)
			Mean (SD)	1.82 (1.471)	5.00 (0.000)
	Week 12	Absolute value	n (%)	8 (66.67)	2 (50.00)
			Number of patients with missing data: n (%)	4 (33.33)	2 (50.00)
			Mean (SD)	1.50 (1.069)	4.00 (1.414)
		Change from Baseline	n (%)	8 (66.67)	2 (50.00)
			Number of patients with missing data: n (%)	4 (33.33)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.26 (0.229)	-0.15 (0.575)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.12 (0.670)	
			95% CI for LS Mean Difference [2]	-1.61, 1.38	
			p-value MMRM [2]	0.8651	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.15	
			95% CI for SMD (Hedges' g)	-1.70, 1.40	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-S communication skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	9 (75.00)	3 (75.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
			Mean (SD)	1.67 (1.118)	3.33 (1.528)
		Change from Baseline	n (%)	9 (75.00)	2 (50.00)
			Number of patients with missing data: n (%)	3 (25.00)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.27 (0.212)	-0.15 (0.569)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.12 (0.650)	
			95% CI for LS Mean Difference [2]	-1.60, 1.35	
			p-value MMRM [2]	0.8524	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.16	
			95% CI for SMD (Hedges' g)	-1.70, 1.37	
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	7 (77.78)	6 (85.71)
			Number of patients with missing data: n (%)	2 (22.22)	1 (14.29)
			Mean (SD)	2.29 (1.113)	2.33 (1.506)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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CaGI-S communication skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	7 (77.78)	5 (71.43)
			Number of patients with missing data: n (%)	2 (22.22)	2 (28.57)
			Mean (SD)	1.86 (1.069)	1.60 (0.894)
		Change from Baseline	n (%)	6 (66.67)	4 (57.14)
			Number of patients with missing data: n (%)	3 (33.33)	3 (42.86)
			LS Mean Change from Baseline (SE) [2]	-0.25 (0.371)	-1.02 (0.441)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.77 (0.576)	
			95% CI for LS Mean Difference [2]	-0.57, 2.11	
			p-value MMRM [2]	0.2182	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.72	
			95% CI for SMD (Hedges' g)	-0.59, 2.04	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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CaGI-S communication skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	7 (77.78)	5 (71.43)
			Number of patients with missing data: n (%)	2 (22.22)	2 (28.57)
			Mean (SD)	2.71 (1.113)	1.60 (0.894)
		Change from Baseline	n (%)	5 (55.56)	4 (57.14)
			Number of patients with missing data: n (%)	4 (44.44)	3 (42.86)
			LS Mean Change from Baseline (SE) [2]	-0.00 (0.350)	-0.89 (0.390)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.89 (0.531)	
			95% CI for LS Mean Difference [2]	-0.34, 2.13	
			p-value MMRM [2]	0.1332	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.94	
			95% CI for SMD (Hedges' g)	-0.46, 2.35	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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4.10.11.23 CaGI-S communication skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.0027 ***	
US	Baseline	Absolute value	n (%)	6 (75.00)	4 (66.67)
			Number of patients with missing data: n (%)	2 (25.00)	2 (33.33)
			Mean (SD)	1.33 (0.816)	2.25 (1.893)
	Week 12	Absolute value	n (%)	7 (87.50)	3 (50.00)
			Number of patients with missing data: n (%)	1 (12.50)	3 (50.00)
			Mean (SD)	1.29 (0.488)	2.67 (2.082)
		Change from Baseline	n (%)	6 (75.00)	3 (50.00)
			Number of patients with missing data: n (%)	2 (25.00)	3 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.04 (0.274)	0.15 (0.408)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.19 (0.506)	
			95% CI for LS Mean Difference [2]	-1.64, 1.26	
			p-value MMRM [2]	0.7244	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.18	
			95% CI for SMD (Hedges' g)	-1.57, 1.21	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S communication skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	7 (87.50)	5 (83.33)
			Number of patients with missing data: n (%)	1 (12.50)	1 (16.67)
			Mean (SD)	1.57 (0.976)	2.20 (1.643)
		Change from Baseline	n (%)	6 (75.00)	4 (66.67)
			Number of patients with missing data: n (%)	2 (25.00)	2 (33.33)
			LS Mean Change from Baseline (SE) [2]	-0.04 (0.224)	0.06 (0.283)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.10 (0.379)	
			95% CI for LS Mean Difference [2]	-0.99, 0.80	
			p-value MMRM [2]	0.8008	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.15	
			95% CI for SMD (Hedges' g)	-1.42, 1.12	
Non-US	Baseline	Absolute value	n (%)	12 (92.31)	4 (80.00)
			Number of patients with missing data: n (%)	1 (7.69)	1 (20.00)
			Mean (SD)	2.33 (1.435)	3.75 (1.500)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S communication skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	8 (61.54)	4 (80.00)
			Number of patients with missing data: n (%)	5 (38.46)	1 (20.00)
			Mean (SD)	2.00 (1.309)	2.00 (1.155)
		Change from Baseline	n (%)	8 (61.54)	3 (60.00)
			Number of patients with missing data: n (%)	5 (38.46)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-0.45 (0.276)	-1.90 (0.463)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.45 (0.551)	
			95% CI for LS Mean Difference [2]	0.23, 2.67	
			p-value MMRM [2]	0.0247 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.62	
			95% CI for SMD (Hedges' g)	0.09, 3.14	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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CaGI-S communication skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	9 (69.23)	3 (60.00)
			Number of patients with missing data: n (%)	4 (30.77)	2 (40.00)
			Mean (SD)	2.56 (1.236)	2.33 (1.155)
		Change from Baseline	n (%)	8 (61.54)	2 (40.00)
			Number of patients with missing data: n (%)	5 (38.46)	3 (60.00)
			LS Mean Change from Baseline (SE) [2]	-0.30 (0.179)	-1.42 (0.374)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.12 (0.418)	
			95% CI for LS Mean Difference [2]	0.12, 2.11	
			p-value MMRM [2]	0.0335 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.78	
			95% CI for SMD (Hedges' g)	0.00, 3.56	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.11.24 CaGI-S communication skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.8571	
I	Baseline	Absolute value	n (%)	8 (88.89)	3 (60.00)
			Number of patients with missing data: n (%)	1 (11.11)	2 (40.00)
			Mean (SD)	1.75 (1.488)	2.67 (2.082)
	Week 12	Absolute value	n (%)	8 (88.89)	3 (60.00)
			Number of patients with missing data: n (%)	1 (11.11)	2 (40.00)
			Mean (SD)	1.63 (1.061)	2.00 (1.000)
		Change from Baseline	n (%)	7 (77.78)	2 (40.00)
			Number of patients with missing data: n (%)	2 (22.22)	3 (60.00)
			LS Mean Change from Baseline (SE) [2]	-0.19 (0.421)	-1.65 (0.742)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.46 (0.857)	
			95% CI for LS Mean Difference [2]	-0.63, 3.55	
			p-value MMRM [2]	0.1386	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.02	
			95% CI for SMD (Hedges' g)	-0.64, 2.68	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S communication skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	7 (77.78)	4 (80.00)
			Number of patients with missing data: n (%)	2 (22.22)	1 (20.00)
			Mean (SD)	1.86 (1.215)	2.00 (0.816)
		Change from Baseline	n (%)	6 (66.67)	2 (40.00)
			Number of patients with missing data: n (%)	3 (33.33)	3 (60.00)
			LS Mean Change from Baseline (SE) [2]	-0.34 (0.221)	-0.48 (0.364)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.14 (0.424)	
			95% CI for LS Mean Difference [2]	-0.94, 1.22	
			p-value MMRM [2]	0.7528	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.20	
			95% CI for SMD (Hedges' g)	-1.40, 1.81	
≥ II	Baseline	Absolute value	n (%)	10 (83.33)	5 (83.33)
			Number of patients with missing data: n (%)	2 (16.67)	1 (16.67)
			Mean (SD)	2.20 (1.229)	3.20 (1.789)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S communication skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	7 (58.33)	4 (66.67)
			Number of patients with missing data: n (%)	5 (41.67)	2 (33.33)
			Mean (SD)	1.71 (1.113)	2.50 (1.915)
		Change from Baseline	n (%)	7 (58.33)	4 (66.67)
			Number of patients with missing data: n (%)	5 (41.67)	2 (33.33)
			LS Mean Change from Baseline (SE) [2]	-0.33 (0.284)	-0.57 (0.390)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.25 (0.495)	
			95% CI for LS Mean Difference [2]	-0.86, 1.35	
			p-value MMRM [2]	0.6311	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.28	
			95% CI for SMD (Hedges' g)	-0.95, 1.52	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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CaGI-S communication skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	9 (75.00)	4 (66.67)
			Number of patients with missing data: n (%)	3 (25.00)	2 (33.33)
			Mean (SD)	2.33 (1.225)	2.50 (1.915)
		Change from Baseline	n (%)	8 (66.67)	4 (66.67)
			Number of patients with missing data: n (%)	4 (33.33)	2 (33.33)
			LS Mean Change from Baseline (SE) [2]	-0.07 (0.229)	-0.57 (0.336)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.51 (0.418)	
			95% CI for LS Mean Difference [2]	-0.43, 1.45	
			p-value MMRM [2]	0.2545	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.67	
			95% CI for SMD (Hedges' g)	-0.56, 1.91	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.11.25 CaGI-S socialization skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.6467	
Male	Baseline	Absolute value	n (%)	11 (91.67)	5 (71.43)
			Number of patients with missing data: n (%)	1 (8.33)	2 (28.57)
			Mean (SD)	1.73 (0.647)	2.60 (0.894)
	Week 12	Absolute value	n (%)	8 (66.67)	3 (42.86)
			Number of patients with missing data: n (%)	4 (33.33)	4 (57.14)
			Mean (SD)	1.25 (0.463)	2.00 (1.732)
		Change from Baseline	n (%)	7 (58.33)	3 (42.86)
			Number of patients with missing data: n (%)	5 (41.67)	4 (57.14)
			LS Mean Change from Baseline (SE) [2]	-0.49 (0.393)	0.39 (0.590)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.88 (0.721)	
			95% CI for LS Mean Difference [2]	-2.50, 0.74	
			p-value MMRM [2]	0.2509	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.73	
			95% CI for SMD (Hedges' g)	-2.13, 0.67	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S socialization skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	8 (66.67)	5 (71.43)
			Number of patients with missing data: n (%)	4 (33.33)	2 (28.57)
			Mean (SD)	1.50 (0.535)	1.80 (1.095)
		Change from Baseline	n (%)	7 (58.33)	4 (57.14)
			Number of patients with missing data: n (%)	5 (41.67)	3 (42.86)
			LS Mean Change from Baseline (SE) [2]	-0.49 (0.298)	0.02 (0.433)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.51 (0.540)	
			95% CI for LS Mean Difference [2]	-1.73, 0.71	
			p-value MMRM [2]	0.3711	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.54	
			95% CI for SMD (Hedges' g)	-1.79, 0.71	
Female	Baseline	Absolute value	n (%)	7 (77.78)	3 (75.00)
			Number of patients with missing data: n (%)	2 (22.22)	1 (25.00)
			Mean (SD)	1.86 (1.215)	3.33 (2.082)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S socialization skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	1.86 (1.069)	1.75 (0.500)
		Change from Baseline	n (%)	7 (77.78)	3 (75.00)
			Number of patients with missing data: n (%)	2 (22.22)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	-0.05 (0.467)	-1.54 (0.717)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.49 (0.862)	
			95% CI for LS Mean Difference [2]	-0.55, 3.52	
			p-value MMRM [2]	0.1275	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.99	
			95% CI for SMD (Hedges' g)	-0.44, 2.43	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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CaGI-S socialization skills by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.25 (1.282)	3.50 (1.291)
		Change from Baseline	n (%)	7 (77.78)	3 (75.00)
			Number of patients with missing data: n (%)	2 (22.22)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	0.09 (0.150)	0.46 (0.243)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.37 (0.303)	
			95% CI for LS Mean Difference [2]	-1.10, 0.36	
			p-value MMRM [2]	0.2656	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.74	
			95% CI for SMD (Hedges' g)	-2.14, 0.66	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.11.26 CaGI-S socialization skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.0501	
<10.5 years old at screening	Baseline	Absolute value	n (%)	11 (91.67)	2 (50.00)
			Number of patients with missing data: n (%)	1 (8.33)	2 (50.00)
			Mean (SD)	1.55 (0.820)	3.00 (1.414)
	Week 12	Absolute value	n (%)	8 (66.67)	2 (50.00)
			Number of patients with missing data: n (%)	4 (33.33)	2 (50.00)
			Mean (SD)	1.38 (0.518)	3.00 (1.414)
		Change from Baseline	n (%)	8 (66.67)	2 (50.00)
			Number of patients with missing data: n (%)	4 (33.33)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.21 (0.328)	0.63 (0.683)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.83 (0.778)	
			95% CI for LS Mean Difference [2]	-2.63, 0.96	
			p-value MMRM [2]	0.3147	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.74	
			95% CI for SMD (Hedges' g)	-2.33, 0.85	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-S socialization skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	9 (75.00)	3 (75.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
			Mean (SD)	1.44 (0.726)	2.67 (1.528)
		Change from Baseline	n (%)	9 (75.00)	2 (50.00)
			Number of patients with missing data: n (%)	3 (25.00)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.22 (0.171)	1.13 (0.427)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.34 (0.481)	
			95% CI for LS Mean Difference [2]	-2.46, -0.23	
			p-value MMRM [2]	0.0239 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-2.15	
			95% CI for SMD (Hedges' g)	-3.98, -0.33	
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	7 (77.78)	6 (85.71)
			Number of patients with missing data: n (%)	2 (22.22)	1 (14.29)
			Mean (SD)	2.14 (0.900)	2.83 (1.472)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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CaGI-S socialization skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	7 (77.78)	5 (71.43)
			Number of patients with missing data: n (%)	2 (22.22)	2 (28.57)
			Mean (SD)	1.71 (1.113)	1.40 (0.548)
		Change from Baseline	n (%)	6 (66.67)	4 (57.14)
			Number of patients with missing data: n (%)	3 (33.33)	3 (42.86)
			LS Mean Change from Baseline (SE) [2]	-0.47 (0.422)	-1.31 (0.526)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.84 (0.683)	
			95% CI for LS Mean Difference [2]	-0.80, 2.47	
			p-value MMRM [2]	0.2624	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.65	
			95% CI for SMD (Hedges' g)	-0.65, 1.96	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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CaGI-S socialization skills by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	7 (77.78)	6 (85.71)
			Number of patients with missing data: n (%)	2 (22.22)	1 (14.29)
			Mean (SD)	2.43 (1.134)	2.50 (1.517)
		Change from Baseline	n (%)	5 (55.56)	5 (71.43)
			Number of patients with missing data: n (%)	4 (44.44)	2 (28.57)
			LS Mean Change from Baseline (SE) [2]	-0.23 (0.487)	-0.13 (0.481)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.11 (0.685)	
			95% CI for LS Mean Difference [2]	-1.76, 1.54	
			p-value MMRM [2]	0.8795	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.08	
			95% CI for SMD (Hedges' g)	-1.32, 1.16	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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4.10.11.27 CaGI-S socialization skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.2507	
US	Baseline	Absolute value	n (%)	6 (75.00)	4 (66.67)
			Number of patients with missing data: n (%)	2 (25.00)	2 (33.33)
			Mean (SD)	1.17 (0.408)	2.00 (0.816)
	Week 12	Absolute value	n (%)	7 (87.50)	3 (50.00)
			Number of patients with missing data: n (%)	1 (12.50)	3 (50.00)
			Mean (SD)	1.29 (0.488)	2.33 (1.528)
		Change from Baseline	n (%)	6 (75.00)	3 (50.00)
			Number of patients with missing data: n (%)	2 (25.00)	3 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.15 (0.425)	1.19 (0.563)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.33 (0.748)	
			95% CI for LS Mean Difference [2]	-3.02, 0.35	
			p-value MMRM [2]	0.1068	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-1.12	
			95% CI for SMD (Hedges' g)	-2.62, 0.39	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S socialization skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	7 (87.50)	5 (83.33)
			Number of patients with missing data: n (%)	1 (12.50)	1 (16.67)
			Mean (SD)	1.29 (0.488)	2.00 (1.000)
		Change from Baseline	n (%)	6 (75.00)	4 (66.67)
			Number of patients with missing data: n (%)	2 (25.00)	2 (33.33)
			LS Mean Change from Baseline (SE) [2]	-0.31 (0.319)	0.79 (0.423)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.10 (0.585)	
			95% CI for LS Mean Difference [2]	-2.47, 0.26	
			p-value MMRM [2]	0.0985	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-1.15	
			95% CI for SMD (Hedges' g)	-2.53, 0.24	
Non-US	Baseline	Absolute value	n (%)	12 (92.31)	4 (80.00)
			Number of patients with missing data: n (%)	1 (7.69)	1 (20.00)
			Mean (SD)	2.08 (0.900)	3.75 (1.258)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S socialization skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	8 (61.54)	4 (80.00)
			Number of patients with missing data: n (%)	5 (38.46)	1 (20.00)
			Mean (SD)	1.75 (1.035)	1.50 (0.577)
		Change from Baseline	n (%)	8 (61.54)	3 (60.00)
			Number of patients with missing data: n (%)	5 (38.46)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-0.50 (0.334)	-2.12 (0.555)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.63 (0.685)	
			95% CI for LS Mean Difference [2]	0.07, 3.18	
			p-value MMRM [2]	0.0426 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.45	
			95% CI for SMD (Hedges' g)	-0.03, 2.94	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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CaGI-S socialization skills by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	9 (69.23)	4 (80.00)
			Number of patients with missing data: n (%)	4 (30.77)	1 (20.00)
			Mean (SD)	2.33 (1.118)	3.25 (1.708)
		Change from Baseline	n (%)	8 (61.54)	3 (60.00)
			Number of patients with missing data: n (%)	5 (38.46)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-0.30 (0.275)	-0.12 (0.490)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.18 (0.584)	
			95% CI for LS Mean Difference [2]	-1.52, 1.17	
			p-value MMRM [2]	0.7672	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.19	
			95% CI for SMD (Hedges' g)	-1.52, 1.14	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.11.28 CaGI-S socialization skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.4990	
I	Baseline	Absolute value	n (%)	8 (88.89)	3 (60.00)
			Number of patients with missing data: n (%)	1 (11.11)	2 (40.00)
			Mean (SD)	1.50 (0.756)	2.67 (2.082)
	Week 12	Absolute value	n (%)	8 (88.89)	3 (60.00)
			Number of patients with missing data: n (%)	1 (11.11)	2 (40.00)
			Mean (SD)	1.38 (0.518)	1.67 (0.577)
		Change from Baseline	n (%)	7 (77.78)	2 (40.00)
			Number of patients with missing data: n (%)	2 (22.22)	3 (60.00)
			LS Mean Change from Baseline (SE) [2]	-0.27 (0.423)	-1.16 (0.881)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.89 (0.990)	
			95% CI for LS Mean Difference [2]	-1.75, 3.54	
			p-value MMRM [2]	0.4138	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.56	
			95% CI for SMD (Hedges' g)	-1.03, 2.16	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S socialization skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	7 (77.78)	5 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	1.57 (0.787)	2.80 (1.483)
		Change from Baseline	n (%)	6 (66.67)	3 (60.00)
			Number of patients with missing data: n (%)	3 (33.33)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-0.26 (0.182)	0.90 (0.264)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.16 (0.337)	
			95% CI for LS Mean Difference [2]	-2.09, -0.23	
			p-value MMRM [2]	0.0256 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-1.79	
			95% CI for SMD (Hedges' g)	-3.46, -0.11	
≥ II	Baseline	Absolute value	n (%)	10 (83.33)	5 (83.33)
			Number of patients with missing data: n (%)	2 (16.67)	1 (16.67)
			Mean (SD)	2.00 (0.943)	3.00 (1.000)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S socialization skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	7 (58.33)	4 (66.67)
			Number of patients with missing data: n (%)	5 (41.67)	2 (33.33)
			Mean (SD)	1.71 (1.113)	2.00 (1.414)
		Change from Baseline	n (%)	7 (58.33)	4 (66.67)
			Number of patients with missing data: n (%)	5 (41.67)	2 (33.33)
			LS Mean Change from Baseline (SE) [2]	-0.32 (0.434)	-0.62 (0.605)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.30 (0.759)	
			95% CI for LS Mean Difference [2]	-1.41, 2.01	
			p-value MMRM [2]	0.7038	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.22	
			95% CI for SMD (Hedges' g)	-1.01, 1.45	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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CaGI-S socialization skills by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	9 (75.00)	4 (66.67)
			Number of patients with missing data: n (%)	3 (25.00)	2 (33.33)
			Mean (SD)	2.11 (1.167)	2.25 (1.500)
		Change from Baseline	n (%)	8 (66.67)	4 (66.67)
			Number of patients with missing data: n (%)	4 (33.33)	2 (33.33)
			LS Mean Change from Baseline (SE) [2]	-0.18 (0.325)	-0.37 (0.478)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.19 (0.597)	
			95% CI for LS Mean Difference [2]	-1.16, 1.54	
			p-value MMRM [2]	0.7619	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.17	
			95% CI for SMD (Hedges' g)	-1.03, 1.38	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.11.29 CaGI-S ability to adapt to environment by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.9805	
Male	Baseline	Absolute value	n (%)	11 (91.67)	5 (71.43)
			Number of patients with missing data: n (%)	1 (8.33)	2 (28.57)
			Mean (SD)	1.73 (0.786)	2.40 (1.517)
	Week 12	Absolute value	n (%)	8 (66.67)	3 (42.86)
			Number of patients with missing data: n (%)	4 (33.33)	4 (57.14)
			Mean (SD)	1.63 (0.744)	2.67 (1.528)
		Change from Baseline	n (%)	7 (58.33)	3 (42.86)
			Number of patients with missing data: n (%)	5 (41.67)	4 (57.14)
			LS Mean Change from Baseline (SE) [2]	-0.14 (0.416)	0.73 (0.650)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.87 (0.793)	
			95% CI for LS Mean Difference [2]	-2.64, 0.91	
			p-value MMRM [2]	0.3012	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.67	
			95% CI for SMD (Hedges' g)	-2.06, 0.72	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S ability to adapt to environment by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	8 (66.67)	5 (71.43)
			Number of patients with missing data: n (%)	4 (33.33)	2 (28.57)
			Mean (SD)	1.50 (0.535)	2.20 (0.837)
		Change from Baseline	n (%)	7 (58.33)	4 (57.14)
			Number of patients with missing data: n (%)	5 (41.67)	3 (42.86)
			LS Mean Change from Baseline (SE) [2]	-0.51 (0.275)	0.23 (0.372)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.74 (0.475)	
			95% CI for LS Mean Difference [2]	-1.83, 0.35	
			p-value MMRM [2]	0.1578	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.86	
			95% CI for SMD (Hedges' g)	-2.15, 0.43	
Female	Baseline	Absolute value	n (%)	7 (77.78)	3 (75.00)
			Number of patients with missing data: n (%)	2 (22.22)	1 (25.00)
			Mean (SD)	1.86 (1.464)	3.33 (2.082)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S ability to adapt to environment by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	2.00 (1.155)	2.25 (1.258)
		Change from Baseline	n (%)	7 (77.78)	3 (75.00)
			Number of patients with missing data: n (%)	2 (22.22)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	-0.02 (0.532)	-0.62 (0.838)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.60 (1.023)	
			95% CI for LS Mean Difference [2]	-1.87, 3.07	
			p-value MMRM [2]	0.5778	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.34	
			95% CI for SMD (Hedges' g)	-1.02, 1.70	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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CaGI-S ability to adapt to environment by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.25 (1.581)	3.25 (1.708)
		Change from Baseline	n (%)	7 (77.78)	3 (75.00)
			Number of patients with missing data: n (%)	2 (22.22)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	-0.02 (0.437)	0.38 (0.697)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.40 (0.860)	
			95% CI for LS Mean Difference [2]	-2.46, 1.66	
			p-value MMRM [2]	0.6565	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.28	
			95% CI for SMD (Hedges' g)	-1.64, 1.08	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.11.30 CaGI-S ability to adapt to environment by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.0820	
<10.5 years old at screening	Baseline	Absolute value	n (%)	11 (91.67)	2 (50.00)
			Number of patients with missing data: n (%)	1 (8.33)	2 (50.00)
			Mean (SD)	1.45 (0.820)	4.00 (0.000)
	Week 12	Absolute value	n (%)	8 (66.67)	2 (50.00)
			Number of patients with missing data: n (%)	4 (33.33)	2 (50.00)
			Mean (SD)	1.63 (0.916)	4.00 (0.000)
		Change from Baseline	n (%)	8 (66.67)	2 (50.00)
			Number of patients with missing data: n (%)	4 (33.33)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	0.03 (0.359)	1.76 (1.046)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.73 (1.237)	
			95% CI for LS Mean Difference [2]	-4.44, 0.98	
			p-value MMRM [2]	0.1881	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-1.44	
			95% CI for SMD (Hedges' g)	-3.14, 0.26	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CaGI-S ability to adapt to environment by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	9 (75.00)	3 (75.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
			Mean (SD)	1.33 (0.707)	3.00 (1.000)
		Change from Baseline	n (%)	9 (75.00)	2 (50.00)
			Number of patients with missing data: n (%)	3 (25.00)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.34 (0.291)	1.26 (0.983)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.59 (1.148)	
			95% CI for LS Mean Difference [2]	-4.23, 1.04	
			p-value MMRM [2]	0.2016	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-1.44	
			95% CI for SMD (Hedges' g)	-3.11, 0.23	
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	7 (77.78)	6 (85.71)
			Number of patients with missing data: n (%)	2 (22.22)	1 (14.29)
			Mean (SD)	2.29 (1.254)	2.33 (1.751)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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CaGI-S ability to adapt to environment by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	7 (77.78)	5 (71.43)
			Number of patients with missing data: n (%)	2 (22.22)	2 (28.57)
			Mean (SD)	2.00 (1.000)	1.80 (0.837)
		Change from Baseline	n (%)	6 (66.67)	4 (57.14)
			Number of patients with missing data: n (%)	3 (33.33)	3 (42.86)
			LS Mean Change from Baseline (SE) [2]	-0.30 (0.450)	-0.80 (0.567)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.50 (0.727)	
			95% CI for LS Mean Difference [2]	-1.27, 2.28	
			p-value MMRM [2]	0.5158	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.36	
			95% CI for SMD (Hedges' g)	-0.92, 1.64	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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CaGI-S ability to adapt to environment by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	7 (77.78)	6 (85.71)
			Number of patients with missing data: n (%)	2 (22.22)	1 (14.29)
			Mean (SD)	2.57 (1.397)	2.50 (1.517)
		Change from Baseline	n (%)	5 (55.56)	5 (71.43)
			Number of patients with missing data: n (%)	4 (44.44)	2 (28.57)
			LS Mean Change from Baseline (SE) [2]	-0.13 (0.651)	-0.08 (0.636)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.05 (0.911)	
			95% CI for LS Mean Difference [2]	-2.27, 2.17	
			p-value MMRM [2]	0.9579	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.03	
			95% CI for SMD (Hedges' g)	-1.27, 1.21	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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4.10.11.31 CaGI-S ability to adapt to environment by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.9549	
US	Baseline	Absolute value	n (%)	6 (75.00)	4 (66.67)
			Number of patients with missing data: n (%)	2 (25.00)	2 (33.33)
			Mean (SD)	1.17 (0.408)	2.50 (1.732)
	Week 12	Absolute value	n (%)	7 (87.50)	3 (50.00)
			Number of patients with missing data: n (%)	1 (12.50)	3 (50.00)
			Mean (SD)	1.43 (0.787)	2.33 (1.528)
		Change from Baseline	n (%)	6 (75.00)	3 (50.00)
			Number of patients with missing data: n (%)	2 (25.00)	3 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.09 (0.513)	0.71 (0.704)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.80 (0.898)	
			95% CI for LS Mean Difference [2]	-2.98, 1.37	
			p-value MMRM [2]	0.4054	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.48	
			95% CI for SMD (Hedges' g)	-1.89, 0.93	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S ability to adapt to environment by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	7 (87.50)	5 (83.33)
			Number of patients with missing data: n (%)	1 (12.50)	1 (16.67)
			Mean (SD)	1.29 (0.488)	2.20 (0.837)
		Change from Baseline	n (%)	6 (75.00)	4 (66.67)
			Number of patients with missing data: n (%)	2 (25.00)	2 (33.33)
			LS Mean Change from Baseline (SE) [2]	-0.42 (0.307)	0.31 (0.384)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.73 (0.547)	
			95% CI for LS Mean Difference [2]	-2.03, 0.56	
			p-value MMRM [2]	0.2213	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.80	
			95% CI for SMD (Hedges' g)	-2.13, 0.52	
Non-US	Baseline	Absolute value	n (%)	12 (92.31)	4 (80.00)
			Number of patients with missing data: n (%)	1 (7.69)	1 (20.00)
			Mean (SD)	2.08 (1.165)	3.00 (1.826)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S ability to adapt to environment by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	8 (61.54)	4 (80.00)
			Number of patients with missing data: n (%)	5 (38.46)	1 (20.00)
			Mean (SD)	2.13 (0.991)	2.50 (1.291)
		Change from Baseline	n (%)	8 (61.54)	3 (60.00)
			Number of patients with missing data: n (%)	5 (38.46)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-0.16 (0.469)	-0.13 (0.769)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.03 (0.929)	
			95% CI for LS Mean Difference [2]	-2.19, 2.14	
			p-value MMRM [2]	0.9773	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.02	
			95% CI for SMD (Hedges' g)	-1.34, 1.31	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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CaGI-S ability to adapt to environment by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	9 (69.23)	4 (80.00)
			Number of patients with missing data: n (%)	4 (30.77)	1 (20.00)
			Mean (SD)	2.33 (1.414)	3.25 (1.708)
		Change from Baseline	n (%)	8 (61.54)	3 (60.00)
			Number of patients with missing data: n (%)	5 (38.46)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-0.27 (0.451)	0.53 (0.759)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.80 (0.897)	
			95% CI for LS Mean Difference [2]	-2.90, 1.30	
			p-value MMRM [2]	0.4003	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.52	
			95% CI for SMD (Hedges' g)	-1.86, 0.83	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.11.32 CaGI-S ability to adapt to environment by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.9308	
I	Baseline	Absolute value	n (%)	8 (88.89)	3 (60.00)
			Number of patients with missing data: n (%)	1 (11.11)	2 (40.00)
			Mean (SD)	1.50 (1.069)	2.33 (2.309)
	Week 12	Absolute value	n (%)	8 (88.89)	3 (60.00)
			Number of patients with missing data: n (%)	1 (11.11)	2 (40.00)
			Mean (SD)	1.75 (0.886)	1.67 (0.577)
		Change from Baseline	n (%)	7 (77.78)	2 (40.00)
			Number of patients with missing data: n (%)	2 (22.22)	3 (60.00)
			LS Mean Change from Baseline (SE) [2]	0.03 (0.382)	-0.59 (0.782)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.62 (0.892)	
			95% CI for LS Mean Difference [2]	-1.57, 2.81	
			p-value MMRM [2]	0.5154	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.47	
			95% CI for SMD (Hedges' g)	-1.12, 2.06	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CaGI-S ability to adapt to environment by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	7 (77.78)	5 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	1.57 (0.787)	2.80 (1.483)
		Change from Baseline	n (%)	6 (66.67)	3 (60.00)
			Number of patients with missing data: n (%)	3 (33.33)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-0.34 (0.486)	1.03 (0.678)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.38 (0.839)	
			95% CI for LS Mean Difference [2]	-3.48, 0.72	
			p-value MMRM [2]	0.1567	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.91	
			95% CI for SMD (Hedges' g)	-2.37, 0.56	
≥ II	Baseline	Absolute value	n (%)	10 (83.33)	5 (83.33)
			Number of patients with missing data: n (%)	2 (16.67)	1 (16.67)
			Mean (SD)	2.00 (1.054)	3.00 (1.414)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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Table Generation: 11SEP2023 1:27:59 PM

CaGI-S ability to adapt to environment by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	7 (58.33)	4 (66.67)
			Number of patients with missing data: n (%)	5 (41.67)	2 (33.33)
			Mean (SD)	1.86 (1.069)	3.00 (1.414)
		Change from Baseline	n (%)	7 (58.33)	4 (66.67)
			Number of patients with missing data: n (%)	5 (41.67)	2 (33.33)
			LS Mean Change from Baseline (SE) [2]	-0.05 (0.495)	-0.18 (0.700)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.13 (0.887)	
			95% CI for LS Mean Difference [2]	-1.99, 2.24	
			p-value MMRM [2]	0.8903	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.08	
			95% CI for SMD (Hedges' g)	-1.15, 1.31	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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CaGI-S ability to adapt to environment by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	9 (75.00)	4 (66.67)
			Number of patients with missing data: n (%)	3 (25.00)	2 (33.33)
			Mean (SD)	2.11 (1.453)	2.50 (1.291)
		Change from Baseline	n (%)	8 (66.67)	4 (66.67)
			Number of patients with missing data: n (%)	4 (33.33)	2 (33.33)
			LS Mean Change from Baseline (SE) [2]	-0.03 (0.320)	-0.68 (0.491)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.65 (0.632)	
			95% CI for LS Mean Difference [2]	-0.79, 2.08	
			p-value MMRM [2]	0.3334	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.60	
			95% CI for SMD (Hedges' g)	-0.63, 1.83	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.12 Subgruppenanalysen für den Endpunkt CGI-S

4.10.12.1 CGI-S ability to walk by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.2019	
Male	Baseline	Absolute value	n (%)	10 (83.33)	3 (42.86)
			Number of patients with missing data: n (%)	2 (16.67)	4 (57.14)
			Mean (SD)	2.70 (1.703)	2.67 (1.155)
	Week 12	Absolute value	n (%)	8 (66.67)	2 (28.57)
			Number of patients with missing data: n (%)	4 (33.33)	5 (71.43)
			Mean (SD)	2.75 (1.753)	3.00 (1.414)
		Change from Baseline	n (%)	8 (66.67)	2 (28.57)
			Number of patients with missing data: n (%)	4 (33.33)	5 (71.43)
			LS Mean Change from Baseline (SE) [2]	0.02 (0.189)	0.22 (0.369)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.20 (0.414)	
			95% CI for LS Mean Difference [2]	-1.16, 0.75	
			p-value MMRM [2]	0.6346	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.32	
			95% CI for SMD (Hedges' g)	-1.88, 1.23	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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1.4.12 CGI-S
CGI-S ability to walk by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	8 (66.67)	4 (57.14)
			Number of patients with missing data: n (%)	4 (33.33)	3 (42.86)
			Mean (SD)	2.88 (1.553)	3.50 (1.291)
		Change from Baseline	n (%)	8 (66.67)	3 (42.86)
			Number of patients with missing data: n (%)	4 (33.33)	4 (57.14)
			LS Mean Change from Baseline (SE) [2]	-0.24 (0.166)	0.31 (0.275)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.56 (0.323)	
			95% CI for LS Mean Difference [2]	-1.29, 0.17	
			p-value MMRM [2]	0.1186	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-1.03	
			95% CI for SMD (Hedges' g)	-2.43, 0.38	
Female	Baseline	Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.50 (1.690)	3.00 (1.826)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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1.4.12 CGI-S
CGI-S ability to walk by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	6 (66.67)	4 (100.00)
			Number of patients with missing data: n (%)	3 (33.33)	0 (0.00)
			Mean (SD)	3.00 (1.549)	2.50 (1.915)
		Change from Baseline	n (%)	6 (66.67)	4 (100.00)
			Number of patients with missing data: n (%)	3 (33.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-0.12 (0.290)	-0.49 (0.344)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.36 (0.449)	
			95% CI for LS Mean Difference [2]	-0.83, 1.56	
			p-value MMRM [2]	0.4573	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.39	
			95% CI for SMD (Hedges' g)	-0.89, 1.67	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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1.4.12 CGI-S
CGI-S ability to walk by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	2.86 (1.864)	2.50 (1.291)
		Change from Baseline	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.12 (0.578)	-0.49 (0.764)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.60 (0.958)	
			95% CI for LS Mean Difference [2]	-1.58, 2.78	
			p-value MMRM [2]	0.5460	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.34	
			95% CI for SMD (Hedges' g)	-0.90, 1.58	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.12.2 CGI-S ability to walk by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.4485	
<10.5 years old at screening	Baseline	Absolute value	n (%)	10 (83.33)	2 (50.00)
			Number of patients with missing data: n (%)	2 (16.67)	2 (50.00)
			Mean (SD)	2.80 (1.814)	3.50 (2.121)
	Week 12	Absolute value	n (%)	7 (58.33)	2 (50.00)
			Number of patients with missing data: n (%)	5 (41.67)	2 (50.00)
			Mean (SD)	2.86 (1.773)	3.50 (2.121)
		Change from Baseline	n (%)	7 (58.33)	2 (50.00)
			Number of patients with missing data: n (%)	5 (41.67)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.28 (0.175)	0.02 (0.329)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.31 (0.373)	
			95% CI for LS Mean Difference [2]	-1.21, 0.60	
			p-value MMRM [2]	0.4431	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.53	
			95% CI for SMD (Hedges' g)	-2.13, 1.06	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CGI-S ability to walk by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	8 (66.67)	3 (75.00)
			Number of patients with missing data: n (%)	4 (33.33)	1 (25.00)
			Mean (SD)	3.00 (1.512)	3.67 (1.528)
		Change from Baseline	n (%)	8 (66.67)	2 (50.00)
			Number of patients with missing data: n (%)	4 (33.33)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.25 (0.226)	-0.48 (0.452)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.22 (0.505)	
			95% CI for LS Mean Difference [2]	-0.99, 1.44	
			p-value MMRM [2]	0.6705	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.29	
			95% CI for SMD (Hedges' g)	-1.27, 1.84	
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	8 (88.89)	5 (71.43)
			Number of patients with missing data: n (%)	1 (11.11)	2 (28.57)
			Mean (SD)	2.38 (1.506)	2.60 (1.342)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CGI-S ability to walk by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	7 (77.78)	4 (57.14)
			Number of patients with missing data: n (%)	2 (22.22)	3 (42.86)
			Mean (SD)	2.86 (1.574)	2.25 (1.500)
		Change from Baseline	n (%)	7 (77.78)	4 (57.14)
			Number of patients with missing data: n (%)	2 (22.22)	3 (42.86)
			LS Mean Change from Baseline (SE) [2]	0.23 (0.219)	-0.51 (0.297)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.74 (0.369)	
			95% CI for LS Mean Difference [2]	-0.12, 1.60	
			p-value MMRM [2]	0.0823	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.06	
			95% CI for SMD (Hedges' g)	-0.26, 2.38	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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CGI-S ability to walk by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	7 (77.78)	5 (71.43)
			Number of patients with missing data: n (%)	2 (22.22)	2 (28.57)
			Mean (SD)	2.71 (1.890)	2.60 (1.140)
		Change from Baseline	n (%)	7 (77.78)	5 (71.43)
			Number of patients with missing data: n (%)	2 (22.22)	2 (28.57)
			LS Mean Change from Baseline (SE) [2]	0.18 (0.574)	-0.00 (0.660)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.18 (0.875)	
			95% CI for LS Mean Difference [2]	-1.78, 2.13	
			p-value MMRM [2]	0.8432	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.10	
			95% CI for SMD (Hedges' g)	-1.04, 1.25	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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4.10.12.3 CGI-S ability to walk by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.4254	
US	Baseline	Absolute value	n (%)	6 (75.00)	3 (50.00)
			Number of patients with missing data: n (%)	2 (25.00)	3 (50.00)
			Mean (SD)	2.67 (1.966)	2.67 (1.155)
	Week 12	Absolute value	n (%)	5 (62.50)	2 (33.33)
			Number of patients with missing data: n (%)	3 (37.50)	4 (66.67)
			Mean (SD)	2.60 (1.817)	2.50 (0.707)
		Change from Baseline	n (%)	5 (62.50)	2 (33.33)
			Number of patients with missing data: n (%)	3 (37.50)	4 (66.67)
	Week 24	Absolute value	n (%)	5 (62.50)	4 (66.67)
			Number of patients with missing data: n (%)	3 (37.50)	2 (33.33)
			Mean (SD)	2.60 (1.817)	3.25 (1.258)
		Change from Baseline	n (%)	5 (62.50)	3 (50.00)
			Number of patients with missing data: n (%)	3 (37.50)	3 (50.00)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

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CGI-S ability to walk by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Baseline	Absolute value	n (%)	12 (92.31)	4 (80.00)
			Number of patients with missing data: n (%)	1 (7.69)	1 (20.00)
			Mean (SD)	2.58 (1.564)	3.00 (1.826)
	Week 12	Absolute value	n (%)	9 (69.23)	4 (80.00)
			Number of patients with missing data: n (%)	4 (30.77)	1 (20.00)
			Mean (SD)	3.00 (1.581)	2.75 (2.062)
		Change from Baseline	n (%)	9 (69.23)	4 (80.00)
			Number of patients with missing data: n (%)	4 (30.77)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	-0.10 (0.368)	-0.24 (0.578)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.14 (0.686)	
			95% CI for LS Mean Difference [2]	-1.33, 1.61	
			p-value MMRM [2]	0.8408	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.12	
			95% CI for SMD (Hedges' g)	-1.06, 1.29	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

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CGI-S ability to walk by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	10 (76.92)	4 (80.00)
			Number of patients with missing data: n (%)	3 (23.08)	1 (20.00)
			Mean (SD)	3.00 (1.633)	2.75 (1.500)
		Change from Baseline	n (%)	10 (76.92)	4 (80.00)
			Number of patients with missing data: n (%)	3 (23.08)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	0.11 (0.358)	-0.24 (0.578)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.35 (0.680)	
			95% CI for LS Mean Difference [2]	-1.12, 1.81	
			p-value MMRM [2]	0.6177	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.28	
			95% CI for SMD (Hedges' g)	-0.89, 1.44	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
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4.10.12.4 CGI-S ability to walk by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.7282	
I	Baseline	Absolute value	n (%)	8 (88.89)	4 (80.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (20.00)
			Mean (SD)	1.88 (1.458)	2.25 (1.258)
	Week 12	Absolute value	n (%)	7 (77.78)	3 (60.00)
			Number of patients with missing data: n (%)	2 (22.22)	2 (40.00)
			Mean (SD)	1.86 (1.464)	1.67 (1.155)
		Change from Baseline	n (%)	7 (77.78)	3 (60.00)
			Number of patients with missing data: n (%)	2 (22.22)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-0.16 (0.169)	-0.51 (0.255)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.34 (0.307)	
			95% CI for LS Mean Difference [2]	-0.40, 1.08	
			p-value MMRM [2]	0.3050	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.62	
			95% CI for SMD (Hedges' g)	-0.77, 2.00	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CGI-S ability to walk by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	6 (66.67)	5 (100.00)
			Number of patients with missing data: n (%)	3 (33.33)	0 (0.00)
			Mean (SD)	1.83 (1.602)	2.80 (1.483)
		Change from Baseline	n (%)	6 (66.67)	4 (80.00)
			Number of patients with missing data: n (%)	3 (33.33)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	-0.33 (0.247)	0.01 (0.306)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.34 (0.394)	
			95% CI for LS Mean Difference [2]	-1.24, 0.56	
			p-value MMRM [2]	0.4068	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.49	
			95% CI for SMD (Hedges' g)	-1.77, 0.80	
≥ II	Baseline	Absolute value	n (%)	10 (83.33)	3 (50.00)
			Number of patients with missing data: n (%)	2 (16.67)	3 (50.00)
			Mean (SD)	3.20 (1.619)	3.67 (1.528)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CGI-S ability to walk by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	7 (58.33)	3 (50.00)
			Number of patients with missing data: n (%)	5 (41.67)	3 (50.00)
			Mean (SD)	3.86 (1.069)	3.67 (1.528)
		Change from Baseline	n (%)	7 (58.33)	3 (50.00)
			Number of patients with missing data: n (%)	5 (41.67)	3 (50.00)
			LS Mean Change from Baseline (SE) [2]	0.06 (0.224)	0.02 (0.337)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.04 (0.404)	
			95% CI for LS Mean Difference [2]	-1.00, 1.07	
			p-value MMRM [2]	0.9309	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.05	
			95% CI for SMD (Hedges' g)	-1.30, 1.40	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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CGI-S ability to walk by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	9 (75.00)	3 (50.00)
			Number of patients with missing data: n (%)	3 (25.00)	3 (50.00)
			Mean (SD)	3.56 (1.333)	3.33 (1.155)
		Change from Baseline	n (%)	9 (75.00)	3 (50.00)
			Number of patients with missing data: n (%)	3 (25.00)	3 (50.00)
			LS Mean Change from Baseline (SE) [2]	0.07 (0.438)	-0.31 (0.759)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.38 (0.876)	
			95% CI for LS Mean Difference [2]	-1.58, 2.35	
			p-value MMRM [2]	0.6723	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.25	
			95% CI for SMD (Hedges' g)	-1.06, 1.57	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.12.5 CGI-S dependance on assistive device by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.6471	
Male	Baseline	Absolute value	n (%)	10 (83.33)	3 (42.86)
			Number of patients with missing data: n (%)	2 (16.67)	4 (57.14)
			Mean (SD)	2.40 (1.713)	2.67 (1.155)
	Week 12	Absolute value	n (%)	7 (58.33)	2 (28.57)
			Number of patients with missing data: n (%)	5 (41.67)	5 (71.43)
			Mean (SD)	2.57 (1.988)	3.00 (1.414)
		Change from Baseline	n (%)	7 (58.33)	2 (28.57)
			Number of patients with missing data: n (%)	5 (41.67)	5 (71.43)
			LS Mean Change from Baseline (SE) [2]	0.03 (0.176)	0.04 (0.356)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.01 (0.398)	
			95% CI for LS Mean Difference [2]	-0.87, 0.84	
			p-value MMRM [2]	0.9722	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.03	
			95% CI for SMD (Hedges' g)	-1.60, 1.54	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

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CGI-S dependance on assistive device by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Week 24	Absolute value	n (%)	7 (58.33)	4 (57.14)
			Number of patients with missing data: n (%)	5 (41.67)	3 (42.86)
			Mean (SD)	2.86 (1.773)	2.75 (1.500)
		Change from Baseline	n (%)	7 (58.33)	3 (42.86)
			Number of patients with missing data: n (%)	5 (41.67)	4 (57.14)
			LS Mean Change from Baseline (SE) [2]	0.00 (0.175)	-0.34 (0.254)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.34 (0.308)	
			95% CI for LS Mean Difference [2]	-0.34, 1.01	
			p-value MMRM [2]	0.2972	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.66	
			95% CI for SMD (Hedges' g)	-0.73, 2.05	
Female	Baseline	Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	2.25 (1.753)	2.00 (2.000)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
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CGI-S dependance on assistive device by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 12	Absolute value	n (%)	6 (66.67)	4 (100.00)
			Number of patients with missing data: n (%)	3 (33.33)	0 (0.00)
			Mean (SD)	3.00 (1.549)	2.00 (2.000)
		Change from Baseline	n (%)	6 (66.67)	4 (100.00)
			Number of patients with missing data: n (%)	3 (33.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-0.02 (0.498)	-0.07 (0.635)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.05 (0.809)	
			95% CI for LS Mean Difference [2]	-1.76, 1.86	
			p-value MMRM [2]	0.9531	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.03	
			95% CI for SMD (Hedges' g)	-1.23, 1.30	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
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CGI-S dependance on assistive device by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Week 24	Absolute value	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	2.86 (1.864)	2.00 (1.414)
		Change from Baseline	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.45 (0.480)	-0.07 (0.635)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.52 (0.796)	
			95% CI for LS Mean Difference [2]	-1.27, 2.32	
			p-value MMRM [2]	0.5279	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.36	
			95% CI for SMD (Hedges' g)	-0.88, 1.60	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
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4.10.12.6 CGI-S dependance on assistive device by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.9352	
<10.5 years old at screening	Baseline	Absolute value	n (%)	10 (83.33)	2 (50.00)
			Number of patients with missing data: n (%)	2 (16.67)	2 (50.00)
			Mean (SD)	2.50 (1.841)	3.50 (2.121)
	Week 12	Absolute value	n (%)	7 (58.33)	2 (50.00)
			Number of patients with missing data: n (%)	5 (41.67)	2 (50.00)
			Mean (SD)	2.71 (1.890)	3.50 (2.121)
		Change from Baseline	n (%)	7 (58.33)	2 (50.00)
			Number of patients with missing data: n (%)	5 (41.67)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.12 (0.135)	0.04 (0.252)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.15 (0.287)	
			95% CI for LS Mean Difference [2]	-0.88, 0.57	
			p-value MMRM [2]	0.6109	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.34	
			95% CI for SMD (Hedges' g)	-1.92, 1.24	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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CGI-S dependance on assistive device by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Week 24	Absolute value	n (%)	8 (66.67)	3 (75.00)
			Number of patients with missing data: n (%)	4 (33.33)	1 (25.00)
			Mean (SD)	2.88 (1.642)	3.00 (1.732)
		Change from Baseline	n (%)	8 (66.67)	2 (50.00)
			Number of patients with missing data: n (%)	4 (33.33)	2 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.01 (0.235)	-0.96 (0.472)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.95 (0.528)	
			95% CI for LS Mean Difference [2]	-0.28, 2.18	
			p-value MMRM [2]	0.1106	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.20	
			95% CI for SMD (Hedges' g)	-0.45, 2.86	
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	8 (88.89)	5 (71.43)
			Number of patients with missing data: n (%)	1 (11.11)	2 (28.57)
			Mean (SD)	2.13 (1.553)	1.80 (1.304)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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CGI-S dependance on assistive device by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 12	Absolute value	n (%)	6 (66.67)	4 (57.14)
			Number of patients with missing data: n (%)	3 (33.33)	3 (42.86)
			Mean (SD)	2.83 (1.722)	1.75 (1.500)
		Change from Baseline	n (%)	6 (66.67)	4 (57.14)
			Number of patients with missing data: n (%)	3 (33.33)	3 (42.86)
			LS Mean Change from Baseline (SE) [2]	0.15 (0.402)	-0.00 (0.487)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.15 (0.635)	
			95% CI for LS Mean Difference [2]	-1.95, 2.25	
			p-value MMRM [2]	0.8294	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.09	
			95% CI for SMD (Hedges' g)	-1.18, 1.36	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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CGI-S dependance on assistive device by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	6 (66.67)	5 (71.43)
			Number of patients with missing data: n (%)	3 (33.33)	2 (28.57)
			Mean (SD)	2.83 (2.041)	2.00 (1.225)
		Change from Baseline	n (%)	6 (66.67)	5 (71.43)
			Number of patients with missing data: n (%)	3 (33.33)	2 (28.57)
			LS Mean Change from Baseline (SE) [2]	0.57 (0.497)	0.17 (0.567)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.40 (0.756)	
			95% CI for LS Mean Difference [2]	-1.29, 2.08	
			p-value MMRM [2]	0.6110	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.28	
			95% CI for SMD (Hedges' g)	-0.91, 1.48	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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4.10.12.7 CGI-S dependance on assistive device by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.7872	
US	Baseline	Absolute value	n (%)	6 (75.00)	3 (50.00)
			Number of patients with missing data: n (%)	2 (25.00)	3 (50.00)
			Mean (SD)	2.33 (2.066)	1.67 (0.577)
	Week 12	Absolute value	n (%)	5 (62.50)	2 (33.33)
			Number of patients with missing data: n (%)	3 (37.50)	4 (66.67)
			Mean (SD)	2.40 (1.949)	1.50 (0.707)
		Change from Baseline	n (%)	5 (62.50)	2 (33.33)
			Number of patients with missing data: n (%)	3 (37.50)	4 (66.67)
			LS Mean Change from Baseline (SE) [2]	-0.16 (0.162)	0.01 (0.248)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.17 (0.303)	
			95% CI for LS Mean Difference [2]	-0.96, 0.61	
			p-value MMRM [2]	0.5901	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.35	
			95% CI for SMD (Hedges' g)	-2.01, 1.30	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CGI-S dependance on assistive device by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Week 24	Absolute value	n (%)	5 (62.50)	4 (66.67)
			Number of patients with missing data: n (%)	3 (37.50)	2 (33.33)
			Mean (SD)	2.40 (1.949)	2.00 (1.414)
		Change from Baseline	n (%)	5 (62.50)	3 (50.00)
			Number of patients with missing data: n (%)	3 (37.50)	3 (50.00)
			LS Mean Change from Baseline (SE) [2]	-0.16 (0.204)	-0.40 (0.267)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.24 (0.341)	
			95% CI for LS Mean Difference [2]	-0.60, 1.09	
			p-value MMRM [2]	0.5022	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.42	
			95% CI for SMD (Hedges' g)	-1.03, 1.87	
Non-US	Baseline	Absolute value	n (%)	12 (92.31)	4 (80.00)
			Number of patients with missing data: n (%)	1 (7.69)	1 (20.00)
			Mean (SD)	2.33 (1.557)	2.75 (2.062)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CGI-S dependance on assistive device by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 12	Absolute value	n (%)	8 (61.54)	4 (80.00)
			Number of patients with missing data: n (%)	5 (38.46)	1 (20.00)
			Mean (SD)	3.00 (1.690)	2.75 (2.062)
		Change from Baseline	n (%)	8 (61.54)	4 (80.00)
			Number of patients with missing data: n (%)	5 (38.46)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	0.11 (0.280)	0.01 (0.413)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.09 (0.499)	
			95% CI for LS Mean Difference [2]	-1.17, 1.36	
			p-value MMRM [2]	0.8562	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.09	
			95% CI for SMD (Hedges' g)	-1.11, 1.29	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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CGI-S dependance on assistive device by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Week 24	Absolute value	n (%)	9 (69.23)	4 (80.00)
			Number of patients with missing data: n (%)	4 (30.77)	1 (20.00)
			Mean (SD)	3.11 (1.691)	2.75 (1.500)
		Change from Baseline	n (%)	9 (69.23)	4 (80.00)
			Number of patients with missing data: n (%)	4 (30.77)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	0.49 (0.397)	0.01 (0.612)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.48 (0.730)	
			95% CI for LS Mean Difference [2]	-1.11, 2.07	
			p-value MMRM [2]	0.5230	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.36	
			95% CI for SMD (Hedges' g)	-0.83, 1.55	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.12.8 CGI-S dependance on assistive device by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.3586	
I	Baseline	Absolute value	n (%)	8 (88.89)	4 (80.00)
			Number of patients with missing data: n (%)	1 (11.11)	1 (20.00)
			Mean (SD)	1.50 (1.414)	1.25 (0.500)
	Week 12	Absolute value	n (%)	7 (77.78)	3 (60.00)
			Number of patients with missing data: n (%)	2 (22.22)	2 (40.00)
			Mean (SD)	1.71 (1.496)	1.00 (0.000)
		Change from Baseline	n (%)	7 (77.78)	3 (60.00)
			Number of patients with missing data: n (%)	2 (22.22)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	0.15 (0.126)	-0.02 (0.202)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.16 (0.239)	
			95% CI for LS Mean Difference [2]	-0.39, 0.72	
			p-value MMRM [2]	0.5130	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.41	
			95% CI for SMD (Hedges' g)	-0.96, 1.78	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CGI-S dependance on assistive device by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Week 24	Absolute value	n (%)	6 (66.67)	5 (100.00)
			Number of patients with missing data: n (%)	3 (33.33)	0 (0.00)
			Mean (SD)	1.67 (1.633)	2.00 (1.225)
		Change from Baseline	n (%)	6 (66.67)	4 (80.00)
			Number of patients with missing data: n (%)	3 (33.33)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	0.00 (0.133)	0.24 (0.159)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.24 (0.208)	
			95% CI for LS Mean Difference [2]	-0.72, 0.24	
			p-value MMRM [2]	0.2850	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.63	
			95% CI for SMD (Hedges' g)	-1.93, 0.68	
≥ II	Baseline	Absolute value	n (%)	10 (83.33)	3 (50.00)
			Number of patients with missing data: n (%)	2 (16.67)	3 (50.00)
			Mean (SD)	3.00 (1.633)	3.67 (1.528)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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CGI-S dependance on assistive device by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 12	Absolute value	n (%)	6 (50.00)	3 (50.00)
			Number of patients with missing data: n (%)	6 (50.00)	3 (50.00)
			Mean (SD)	4.00 (1.095)	3.67 (1.528)
		Change from Baseline	n (%)	6 (50.00)	3 (50.00)
			Number of patients with missing data: n (%)	6 (50.00)	3 (50.00)
			LS Mean Change from Baseline (SE) [2]	0.15 (0.339)	0.02 (0.428)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.12 (0.544)	
			95% CI for LS Mean Difference [2]	-1.23, 1.47	
			p-value MMRM [2]	0.8294	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.12	
			95% CI for SMD (Hedges' g)	-1.27, 1.51	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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CGI-S dependance on assistive device by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Week 24	Absolute value	n (%)	8 (66.67)	3 (50.00)
			Number of patients with missing data: n (%)	4 (33.33)	3 (50.00)
			Mean (SD)	3.75 (1.282)	3.00 (1.732)
		Change from Baseline	n (%)	8 (66.67)	3 (50.00)
			Number of patients with missing data: n (%)	4 (33.33)	3 (50.00)
			LS Mean Change from Baseline (SE) [2]	0.30 (0.454)	-0.64 (0.739)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.94 (0.867)	
			95% CI for LS Mean Difference [2]	-1.04, 2.92	
			p-value MMRM [2]	0.3082	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.63	
			95% CI for SMD (Hedges' g)	-0.73, 1.99	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Covariance structure type=compound symmetry.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.13 Subgruppenanalysen für den Endpunkt 9HPT

4.10.13.1 Summary of Z-scores from 9-Hole Pegboard Test by gender

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.1774	
	Male	Baseline	Absolute value	n (%)	10 (83.33)	7 (100.00)
				Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
				Mean (SD)	2.22 (2.989)	3.17 (3.259)
				Median (MAD)	1.99 (1.660)	3.12 (2.300)
		Week 12	Absolute value	n (%)	9 (75.00)	7 (100.00)
				Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
				Mean (SD)	2.97 (2.066)	3.20 (1.926)
				Median (MAD)	2.40 (1.600)	3.20 (1.850)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

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1.4.13 Other morbidity assessments
Summary of Z-scores from 9-Hole Pegboard Test by gender

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	Male	Week 12	Change from Baseline	n (%)	9 (75.00)	7 (100.00)
				Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	0.12 (0.54)	0.16 (0.62)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.03 (0.82)	
				95% CI for LS Mean Difference [2]	-1.81, 1.74	
				p-value MMRM [2]	0.9669	
				Mean (SD)	0.27 (2.301)	0.03 (2.358)
				Median (MAD)	-0.70 (0.650)	0.41 (0.920)
				Mean Difference (SE) [3]	0.24 (1.172)	
				95% CI for Mean Difference [3]	-2.30, 2.78	
				p-value (Welch's t-test) [3]	0.8424	
				Median Difference (ASE) [4]	0.63 (1.362)	
				95% CI for Median Difference [4]	-3.11, 2.08	
				p-value (Mann-Whitney U test)	0.6720	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.10	
				95% CI for SMD (Hedges' g)	-0.89, 1.09	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
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1.4.13 Other morbidity assessments
Summary of Z-scores from 9-Hole Pegboard Test by gender

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	Male	Week 24	Absolute value	n (%)	8 (66.67)	7 (100.00)
				Number of patients with missing data: n (%)	4 (33.33)	0 (0.00)
				Mean (SD)	4.52 (4.318)	4.15 (3.276)
				Median (MAD)	3.03 (3.020)	4.05 (2.490)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
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1.4.13 Other morbidity assessments
Summary of Z-scores from 9-Hole Pegboard Test by gender

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	Male	Week 24	Change from Baseline	n (%)	8 (66.67)	7 (100.00)
				Number of patients with missing data: n (%)	4 (33.33)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	1.38 (1.24)	1.12 (1.34)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.27 (1.82)	
				95% CI for LS Mean Difference [2]	-3.67, 4.20	
				p-value MMRM [2]	0.8862	
				Mean (SD)	1.67 (4.892)	0.99 (1.457)
				Median (MAD)	-0.38 (0.700)	0.74 (1.110)
				Mean Difference (SE) [3]	0.68 (1.927)	
				95% CI for Mean Difference [3]	-3.47, 4.83	
				p-value (Welch's t-test) [3]	0.7162	
				Median Difference (ASE) [4]	0.86 (1.776)	
				95% CI for Median Difference [4]	-4.26, 2.70	
				p-value (Mann-Whitney U test)	0.4519	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.18	
				95% CI for SMD (Hedges' g)	-0.83, 1.20	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
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1.4.13 Other morbidity assessments
Summary of Z-scores from 9-Hole Pegboard Test by gender

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	Female	Baseline	Absolute value	n (%)	8 (88.89)	4 (100.00)
				Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
				Mean (SD)	2.20 (1.552)	27.82 (44.678)
				Median (MAD)	2.68 (1.235)	7.65 (4.860)
		Week 12	Absolute value	n (%)	7 (77.78)	4 (100.00)
				Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
				Mean (SD)	2.46 (2.408)	5.90 (5.252)
				Median (MAD)	2.16 (2.040)	4.09 (1.295)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
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1.4.13 Other morbidity assessments
Summary of Z-scores from 9-Hole Pegboard Test by gender

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	Female	Week 12	Change from Baseline	n (%)	7 (77.78)	4 (100.00)
				Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	-9.06 (1.36)	-5.20 (1.97)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-3.86 (2.55)	
				95% CI for LS Mean Difference [2]	-9.58, 1.86	
				p-value MMRM [2]	0.1625	
				Mean (SD)	0.56 (2.756)	-21.92 (45.913)
				Median (MAD)	1.02 (1.180)	0.32 (1.105)
				Mean Difference (SE) [3]	22.48 (16.674)	
				95% CI for Mean Difference [3]	-50.48, 95.44	
				p-value (Welch's t-test) [3]	0.3998	
				Median Difference (ASE) [4]	-0.95 (24.745)	
				95% CI for Median Difference [4]	-91.79, 2.98	
				p-value (Mann-Whitney U test)	0.7768	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.85	
				95% CI for SMD (Hedges' g)	-0.44, 2.13	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
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1.4.13 Other morbidity assessments
Summary of Z-scores from 9-Hole Pegboard Test by gender

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	Female	Week 24	Absolute value	n (%)	7 (77.78)	4 (100.00)
				Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
				Mean (SD)	2.67 (1.914)	4.15 (5.173)
				Median (MAD)	2.50 (1.800)	2.00 (0.685)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
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1.4.13 Other morbidity assessments
Summary of Z-scores from 9-Hole Pegboard Test by gender

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	Female	Week 24	Change from Baseline	n (%)	7 (77.78)	4 (100.00)
				Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	-8.68 (1.31)	-6.94 (1.90)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.74 (2.46)	
				95% CI for LS Mean Difference [2]	-7.31, 3.83	
				p-value MMRM [2]	0.4976	
				Mean (SD)	0.28 (1.739)	-23.66 (46.046)
				Median (MAD)	0.41 (0.610)	-1.35 (2.060)
				Mean Difference (SE) [3]	23.94 (16.686)	
				95% CI for Mean Difference [3]	-49.29, 97.17	
				p-value (Welch's t-test) [3]	0.3749	
				Median Difference (ASE) [4]	-1.50 (24.131)	
				95% CI for Median Difference [4]	-93.08, 0.88	
				p-value (Mann-Whitney U test)	0.2986	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.90	
				95% CI for SMD (Hedges' g)	-0.40, 2.20	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
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1.4.13 Other morbidity assessments
Summary of Z-scores from 9-Hole Pegboard Test by gender

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.2191	
	Male	Baseline	Absolute value	n (%)	10 (83.33)	7 (100.00)
				Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
				Mean (SD)	3.71 (4.203)	4.85 (5.459)
				Median (MAD)	3.41 (1.395)	4.54 (2.670)
		Week 12	Absolute value	n (%)	8 (66.67)	6 (85.71)
				Number of patients with missing data: n (%)	4 (33.33)	1 (14.29)
				Mean (SD)	7.72 (9.834)	3.91 (2.387)
				Median (MAD)	5.25 (3.415)	4.65 (1.380)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
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1.4.13 Other morbidity assessments
Summary of Z-scores from 9-Hole Pegboard Test by gender

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	Male	Week 12	Change from Baseline	n (%)	8 (66.67)	6 (85.71)
				Number of patients with missing data: n (%)	4 (33.33)	1 (14.29)
				LS Mean Change from Baseline (SE) [2]	3.36 (1.79)	0.67 (2.07)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.69 (2.74)	
				95% CI for LS Mean Difference [2]	-3.43, 8.80	
				p-value MMRM [2]	0.3499	
				Mean (SD)	3.43 (5.952)	0.93 (2.150)
				Median (MAD)	2.00 (2.015)	0.49 (1.280)
				Mean Difference (SE) [3]	2.50 (2.567)	
				95% CI for Mean Difference [3]	-2.63, 7.64	
				p-value (Welch's t-test) [3]	0.2999	
				Median Difference (ASE) [4]	-1.10 (2.082)	
				95% CI for Median Difference [4]	-5.18, 1.90	
				p-value (Mann-Whitney U test)	0.3329	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.53	
				95% CI for SMD (Hedges' g)	-0.55, 1.61	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
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1.4.13 Other morbidity assessments
Summary of Z-scores from 9-Hole Pegboard Test by gender

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	Male	Week 24	Absolute value	n (%)	8 (66.67)	7 (100.00)
				Number of patients with missing data: n (%)	4 (33.33)	0 (0.00)
				Mean (SD)	6.75 (5.265)	5.37 (4.237)
				Median (MAD)	8.00 (3.465)	3.36 (2.610)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
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1.4.13 Other morbidity assessments
Summary of Z-scores from 9-Hole Pegboard Test by gender

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	Male	Week 24	Change from Baseline	n (%)	8 (66.67)	7 (100.00)
				Number of patients with missing data: n (%)	4 (33.33)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	2.42 (1.11)	0.58 (1.18)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.84 (1.62)	
				95% CI for LS Mean Difference [2]	-1.73, 5.41	
				p-value MMRM [2]	0.2809	
				Mean (SD)	2.50 (3.381)	0.52 (2.791)
				Median (MAD)	1.54 (2.095)	1.92 (1.840)
				Mean Difference (SE) [3]	1.98 (1.616)	
				95% CI for Mean Difference [3]	-1.47, 5.42	
				p-value (Welch's t-test) [3]	0.2370	
				Median Difference (ASE) [4]	-1.63 (2.079)	
				95% CI for Median Difference [4]	-5.82, 2.33	
				p-value (Mann-Whitney U test)	0.3854	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.63	
				95% CI for SMD (Hedges' g)	-0.41, 1.68	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
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1.4.13 Other morbidity assessments
Summary of Z-scores from 9-Hole Pegboard Test by gender

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	Female	Baseline	Absolute value	n (%)	8 (88.89)	4 (100.00)
				Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
				Mean (SD)	2.29 (2.558)	38.02 (58.427)
				Median (MAD)	1.02 (1.035)	12.25 (8.025)
		Week 12	Absolute value	n (%)	7 (77.78)	4 (100.00)
				Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
				Mean (SD)	3.89 (5.420)	7.87 (10.570)
				Median (MAD)	1.78 (0.520)	3.89 (1.900)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
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1.4.13 Other morbidity assessments
Summary of Z-scores from 9-Hole Pegboard Test by gender

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	Female	Week 12	Change from Baseline	n (%)	7 (77.78)	4 (100.00)
				Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	-12.68 (2.84)	-5.16 (4.07)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-7.51 (5.17)	
				95% CI for LS Mean Difference [2]	-19.02, 3.99	
				p-value MMRM [2]	0.1766	
				Mean (SD)	2.19 (5.950)	-30.14 (60.836)
				Median (MAD)	0.51 (1.410)	-2.12 (3.630)
				Mean Difference (SE) [3]	32.33 (22.225)	
				95% CI for Mean Difference [3]	-64.15, 128.81	
				p-value (Welch's t-test) [3]	0.3662	
				Median Difference (ASE) [4]	-3.11 (32.567)	
				95% CI for Median Difference [4]	-121.77, 4.42	
				p-value (Mann-Whitney U test)	0.2986	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.91	
				95% CI for SMD (Hedges' g)	-0.39, 2.21	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
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1.4.13 Other morbidity assessments
Summary of Z-scores from 9-Hole Pegboard Test by gender

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	Female	Week 24	Absolute value	n (%)	7 (77.78)	4 (100.00)
				Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
				Mean (SD)	2.90 (2.282)	7.43 (8.818)
				Median (MAD)	2.98 (1.420)	4.34 (1.930)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
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1.4.13 Other morbidity assessments
Summary of Z-scores from 9-Hole Pegboard Test by gender

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	Female	Week 24	Change from Baseline	n (%)	7 (77.78)	4 (100.00)
				Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	-12.19 (2.29)	-5.61 (3.31)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-6.58 (4.28)	
				95% CI for LS Mean Difference [2]	-16.35, 3.18	
				p-value MMRM [2]	0.1601	
				Mean (SD)	0.36 (2.110)	-30.59 (62.563)
				Median (MAD)	-0.02 (1.940)	0.04 (1.855)
				Mean Difference (SE) [3]	30.95 (22.666)	
				95% CI for Mean Difference [3]	-68.56, 130.46	
				p-value (Welch's t-test) [3]	0.3954	
				Median Difference (ASE) [4]	-0.78 (32.909)	
				95% CI for Median Difference [4]	-124.38, 2.52	
				p-value (Mann-Whitney U test)	0.5083	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.86	
				95% CI for SMD (Hedges' g)	-0.43, 2.15	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
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4.10.13.2 Summary of Z-scores from 9-Hole Pegboard Test by age group

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.0293 ***	
	<10.5 years old at screening	Baseline	Absolute value	n (%)	9 (75.00)	4 (100.00)
				Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
				Mean (SD)	1.71 (1.977)	4.98 (4.438)
				Median (MAD)	2.68 (0.970)	4.09 (1.930)
		Week 12	Absolute value	n (%)	8 (66.67)	4 (100.00)
				Number of patients with missing data: n (%)	4 (33.33)	0 (0.00)
				Mean (SD)	1.92 (1.753)	6.20 (5.299)
				Median (MAD)	2.28 (0.995)	5.10 (2.075)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Median age used as cut-off point.

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Summary of Z-scores from 9-Hole Pegboard Test by age group

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	<10.5 years old at screening	Week 12	Change from Baseline	n (%)	8 (66.67)	4 (100.00)
				Number of patients with missing data: n (%)	4 (33.33)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	-0.24 (0.70)	1.17 (1.03)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.41 (1.31)	
				95% CI for LS Mean Difference [2]	-4.33, 1.50	
				p-value MMRM [2]	0.3050	
				Mean (SD)	-0.27 (2.092)	1.22 (0.908)
				Median (MAD)	-0.34 (1.135)	1.02 (0.460)
				Mean Difference (SE) [3]	1.49 (1.114)	
				95% CI for Mean Difference [3]	-0.44, 3.43	
				p-value (Welch's t-test) [3]	0.1158	
				Median Difference (ASE) [4]	1.33 (1.541)	
				95% CI for Median Difference [4]	-0.76, 3.71	
				p-value (Mann-Whitney U test)	0.2027	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.82	
				95% CI for SMD (Hedges' g)	-2.07, 0.43	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Median age used as cut-off point.

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Summary of Z-scores from 9-Hole Pegboard Test by age group

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	<10.5 years old at screening	Week 24	Absolute value	n (%)	8 (66.67)	4 (100.00)
				Number of patients with missing data: n (%)	4 (33.33)	0 (0.00)
				Mean (SD)	2.80 (2.933)	6.01 (5.005)
				Median (MAD)	1.94 (1.630)	5.98 (3.840)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
NOTE: Median age used as cut-off point.
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Summary of Z-scores from 9-Hole Pegboard Test by age group

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	<10.5 years old at screening	Week 24	Change from Baseline	n (%)	8 (66.67)	4 (100.00)
				Number of patients with missing data: n (%)	4 (33.33)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	0.64 (0.81)	0.98 (1.19)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.34 (1.49)	
				95% CI for LS Mean Difference [2]	-3.63, 2.96	
				p-value MMRM [2]	0.8264	
				Mean (SD)	0.62 (2.361)	1.03 (1.674)
				Median (MAD)	0.46 (0.995)	0.52 (0.545)
				Mean Difference (SE) [3]	0.42 (1.334)	
				95% CI for Mean Difference [3]	-2.29, 3.12	
				p-value (Welch's t-test) [3]	0.7326	
				Median Difference (ASE) [4]	0.26 (1.584)	
				95% CI for Median Difference [4]	-1.88, 3.47	
				p-value (Mann-Whitney U test)	0.9323	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.19	
				95% CI for SMD (Hedges' g)	-1.39, 1.01	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Median age used as cut-off point.

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Summary of Z-scores from 9-Hole Pegboard Test by age group

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	9 (100.00)	7 (100.00)
				Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
				Mean (SD)	2.71 (2.773)	16.22 (34.684)
				Median (MAD)	2.48 (1.820)	3.12 (2.300)
		Week 12	Absolute value	n (%)	8 (88.89)	7 (100.00)
				Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
				Mean (SD)	3.57 (2.313)	3.02 (1.510)
				Median (MAD)	4.36 (1.770)	3.20 (1.200)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Median age used as cut-off point.

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Program: t-qs-cont-peg9-sub.sas

Summary of Z-scores from 9-Hole Pegboard Test by age group

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	≥ 10.5 years old at screening	Week 12	Change from Baseline	n (%)	8 (88.89)	7 (100.00)
				Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	-5.60 (0.72)	-6.37 (0.78)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.76 (1.09)	
				95% CI for LS Mean Difference [2]	-1.58, 3.11	
				p-value MMRM [2]	0.4940	
				Mean (SD)	1.07 (2.685)	-13.19 (34.283)
				Median (MAD)	0.41 (1.435)	-0.07 (0.820)
				Mean Difference (SE) [3]	14.26 (12.097)	
				95% CI for Mean Difference [3]	-17.45, 45.97	
				p-value (Welch's t-test) [3]	0.3140	
				Median Difference (ASE) [4]	-1.43 (2.051)	
				95% CI for Median Difference [4]	-6.44, 1.60	
				p-value (Mann-Whitney U test)	0.3854	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.61	
				95% CI for SMD (Hedges' g)	-0.43, 1.65	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Median age used as cut-off point.

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Summary of Z-scores from 9-Hole Pegboard Test by age group

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	7 (77.78)	7 (100.00)
				Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
				Mean (SD)	4.63 (3.927)	3.09 (2.825)
				Median (MAD)	4.28 (2.210)	1.88 (0.320)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
NOTE: Median age used as cut-off point.
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Summary of Z-scores from 9-Hole Pegboard Test by age group

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	≥ 10.5 years old at screening	Week 24	Change from Baseline	n (%)	7 (77.78)	7 (100.00)
				Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	-4.70 (1.32)	-6.30 (1.36)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.60 (1.91)	
				95% CI for LS Mean Difference [2]	-2.54, 5.73	
				p-value MMRM [2]	0.4184	
				Mean (SD)	1.48 (5.018)	-13.12 (35.123)
				Median (MAD)	-0.35 (0.330)	0.70 (1.250)
				Mean Difference (SE) [3]	14.61 (13.410)	
				95% CI for Mean Difference [3]	-17.90, 47.11	
				p-value (Welch's t-test) [3]	0.3163	
				Median Difference (ASE) [4]	0.35 (3.903)	
				95% CI for Median Difference [4]	-1.99, 13.31	
				p-value (Mann-Whitney U test)	0.7983	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.58	
				95% CI for SMD (Hedges' g)	-0.49, 1.66	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Median age used as cut-off point.

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Summary of Z-scores from 9-Hole Pegboard Test by age group

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.2444	
	<10.5 years old at screening	Baseline	Absolute value	n (%)	9 (75.00)	4 (100.00)
				Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
				Mean (SD)	2.97 (4.432)	7.46 (7.847)
				Median (MAD)	1.28 (1.830)	5.57 (2.810)
		Week 12	Absolute value	n (%)	7 (58.33)	4 (100.00)
				Number of patients with missing data: n (%)	5 (41.67)	0 (0.00)
				Mean (SD)	5.85 (10.922)	9.13 (9.892)
				Median (MAD)	1.78 (0.520)	5.93 (2.950)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
NOTE: Median age used as cut-off point.
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Summary of Z-scores from 9-Hole Pegboard Test by age group

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	<10.5 years old at screening	Week 12	Change from Baseline	n (%)	7 (58.33)	4 (100.00)
				Number of patients with missing data: n (%)	5 (41.67)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	2.71 (1.93)	1.33 (2.54)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.39 (3.20)	
				95% CI for LS Mean Difference [2]	-5.97, 8.74	
				p-value MMRM [2]	0.6763	
				Mean (SD)	2.42 (6.525)	1.67 (2.439)
				Median (MAD)	0.51 (1.410)	1.34 (1.295)
				Mean Difference (SE) [3]	-0.75 (3.454)	
				95% CI for Mean Difference [3]	-7.06, 5.55	
				p-value (Welch's t-test) [3]	0.7908	
				Median Difference (ASE) [4]	0.74 (5.107)	
				95% CI for Median Difference [4]	-11.87, 4.42	
				p-value (Mann-Whitney U test)	0.6366	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.14	
				95% CI for SMD (Hedges' g)	-1.09, 1.37	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Median age used as cut-off point.

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Summary of Z-scores from 9-Hole Pegboard Test by age group

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	<10.5 years old at screening	Week 24	Absolute value	n (%)	8 (66.67)	4 (100.00)
				Number of patients with missing data: n (%)	4 (33.33)	0 (0.00)
				Mean (SD)	4.83 (4.880)	9.01 (8.175)
				Median (MAD)	3.18 (2.525)	6.43 (3.360)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
NOTE: Median age used as cut-off point.
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Summary of Z-scores from 9-Hole Pegboard Test by age group

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	<10.5 years old at screening	Week 24	Change from Baseline	n (%)	8 (66.67)	4 (100.00)
				Number of patients with missing data: n (%)	4 (33.33)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	1.59 (0.75)	1.21 (1.08)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.38 (1.35)	
				95% CI for LS Mean Difference [2]	-2.72, 3.48	
				p-value MMRM [2]	0.7832	
				Mean (SD)	1.41 (1.534)	1.55 (2.521)
				Median (MAD)	1.64 (1.300)	2.24 (0.975)
				Mean Difference (SE) [3]	0.13 (1.155)	
				95% CI for Mean Difference [3]	-3.62, 3.89	
				p-value (Welch's t-test) [3]	0.9262	
				Median Difference (ASE) [4]	0.44 (1.870)	
				95% CI for Median Difference [4]	-3.40, 2.68	
				p-value (Mann-Whitney U test)	0.9323	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.07	
				95% CI for SMD (Hedges' g)	-1.27, 1.13	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Median age used as cut-off point.

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Summary of Z-scores from 9-Hole Pegboard Test by age group

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	9 (100.00)	7 (100.00)
				Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
				Mean (SD)	3.19 (2.653)	22.31 (45.596)
				Median (MAD)	3.55 (2.380)	4.54 (2.670)
		Week 12	Absolute value	n (%)	8 (88.89)	6 (85.71)
				Number of patients with missing data: n (%)	1 (11.11)	1 (14.29)
				Mean (SD)	6.01 (5.238)	3.07 (1.990)
				Median (MAD)	5.45 (3.210)	3.89 (0.855)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Median age used as cut-off point.

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Summary of Z-scores from 9-Hole Pegboard Test by age group

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	≥ 10.5 years old at screening	Week 12	Change from Baseline	n (%)	8 (88.89)	6 (85.71)
				Number of patients with missing data: n (%)	1 (11.11)	1 (14.29)
				LS Mean Change from Baseline (SE) [2]	-6.47 (1.61)	-8.23 (1.84)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.76 (2.54)	
				95% CI for LS Mean Difference [2]	-3.78, 7.30	
				p-value MMRM [2]	0.5013	
				Mean (SD)	3.22 (5.455)	-20.28 (49.535)
				Median (MAD)	2.00 (2.045)	-1.41 (1.140)
				Mean Difference (SE) [3]	23.51 (17.414)	
				95% CI for Mean Difference [3]	-28.43, 75.45	
				p-value (Welch's t-test) [3]	0.2986	
				Median Difference (ASE) [4]	-3.62 (30.447)	
				95% CI for Median Difference [4]	-17.55, 0.68	
				p-value (Mann-Whitney U test)	0.0814	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.73	
				95% CI for SMD (Hedges' g)	-0.37, 1.83	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Median age used as cut-off point.

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Summary of Z-scores from 9-Hole Pegboard Test by age group

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	7 (77.78)	7 (100.00)
				Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
				Mean (SD)	5.11 (4.352)	4.46 (4.056)
				Median (MAD)	4.40 (4.300)	4.17 (2.290)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
NOTE: Median age used as cut-off point.
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Summary of Z-scores from 9-Hole Pegboard Test by age group

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	≥ 10.5 years old at screening	Week 24	Change from Baseline	n (%)	7 (77.78)	7 (100.00)
				Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	-6.38 (1.88)	-7.84 (2.03)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.46 (2.85)	
				95% CI for LS Mean Difference [2]	-4.95, 7.87	
				p-value MMRM [2]	0.6194	
				Mean (SD)	1.60 (4.225)	-17.85 (47.039)
				Median (MAD)	-0.20 (1.910)	-1.12 (3.040)
				Mean Difference (SE) [3]	19.44 (17.851)	
				95% CI for Mean Difference [3]	-24.07, 62.96	
				p-value (Welch's t-test) [3]	0.3172	
				Median Difference (ASE) [4]	2.83 (3.373)	
				95% CI for Median Difference [4]	-2.35, 10.87	
				p-value (Mann-Whitney U test)	0.3711	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.58	
				95% CI for SMD (Hedges' g)	-0.49, 1.66	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Median age used as cut-off point.

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4.10.13.3 Summary of Z-scores from 9-Hole Pegboard Test by region

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.4215	
	US	Baseline	Absolute value	n (%)	6 (75.00)	6 (100.00)
				Number of patients with missing data: n (%)	2 (25.00)	0 (0.00)
				Mean (SD)	1.94 (1.617)	2.81 (1.691)
				Median (MAD)	2.58 (0.630)	3.42 (0.880)
		Week 12	Absolute value	n (%)	6 (75.00)	6 (100.00)
				Number of patients with missing data: n (%)	2 (25.00)	0 (0.00)
				Mean (SD)	2.41 (2.282)	3.10 (2.019)
				Median (MAD)	2.48 (1.985)	3.32 (1.785)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

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Summary of Z-scores from 9-Hole Pegboard Test by region

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	US	Week 12	Change from Baseline	n (%)	6 (75.00)	6 (100.00)
				Number of patients with missing data: n (%)	2 (25.00)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	0.13 (0.94)	0.62 (0.94)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.48 (1.36)	
				95% CI for LS Mean Difference [2]	-3.56, 2.59	
				p-value MMRM [2]	0.7307	
				Mean (SD)	0.46 (3.481)	0.29 (0.747)
				Median (MAD)	0.67 (1.920)	0.33 (0.385)
				Mean Difference (SE) [3]	0.18 (1.454)	
				95% CI for Mean Difference [3]	-3.47, 3.82	
				p-value (Welch's t-test) [3]	0.9085	
				Median Difference (ASE) [4]	0.46 (2.357)	
				95% CI for Median Difference [4]	-3.57, 4.22	
				p-value (Mann-Whitney U test)	0.9362	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.07	
				95% CI for SMD (Hedges' g)	-1.06, 1.20	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

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Summary of Z-scores from 9-Hole Pegboard Test by region

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	US	Week 24	Absolute value	n (%)	6 (75.00)	6 (100.00)
				Number of patients with missing data: n (%)	2 (25.00)	0 (0.00)
				Mean (SD)	3.63 (4.346)	3.26 (2.962)
				Median (MAD)	2.29 (2.075)	2.81 (2.160)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
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Summary of Z-scores from 9-Hole Pegboard Test by region

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	US	Week 24	Change from Baseline	n (%)	6 (75.00)	6 (100.00)
				Number of patients with missing data: n (%)	2 (25.00)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	1.36 (1.59)	0.78 (1.59)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.58 (2.27)	
				95% CI for LS Mean Difference [2]	-4.48, 5.64	
				p-value MMRM [2]	0.8030	
				Mean (SD)	1.69 (5.588)	0.45 (2.317)
				Median (MAD)	-0.30 (1.555)	0.54 (1.160)
				Mean Difference (SE) [3]	1.24 (2.470)	
				95% CI for Mean Difference [3]	-4.66, 7.14	
				p-value (Welch's t-test) [3]	0.6322	
				Median Difference (ASE) [4]	-0.52 (3.689)	
				95% CI for Median Difference [4]	-3.63, 9.10	
				p-value (Mann-Whitney U test)	0.8102	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.29	
				95% CI for SMD (Hedges' g)	-0.85, 1.43	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

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Summary of Z-scores from 9-Hole Pegboard Test by region

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	Non-US	Baseline	Absolute value	n (%)	12 (92.31)	5 (100.00)
				Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
				Mean (SD)	2.34 (2.756)	23.31 (40.117)
				Median (MAD)	2.09 (1.660)	9.46 (8.040)
		Week 12	Absolute value	n (%)	10 (76.92)	5 (100.00)
				Number of patients with missing data: n (%)	3 (23.08)	0 (0.00)
				Mean (SD)	2.95 (2.181)	5.48 (4.683)
				Median (MAD)	2.40 (1.650)	3.78 (1.220)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

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Summary of Z-scores from 9-Hole Pegboard Test by region

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	Non-US	Week 12	Change from Baseline	n (%)	10 (76.92)	5 (100.00)
				Number of patients with missing data: n (%)	3 (23.08)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	-6.99 (1.04)	-4.26 (1.55)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-2.72 (1.96)	
				95% CI for LS Mean Difference [2]	-6.94, 1.50	
				p-value MMRM [2]	0.1868	
				Mean (SD)	0.36 (1.752)	-17.84 (40.881)
				Median (MAD)	-0.21 (1.090)	0.39 (2.810)
				Mean Difference (SE) [3]	18.20 (12.446)	
				95% CI for Mean Difference [3]	-32.55, 68.94	
				p-value (Welch's t-test) [3]	0.3760	
				Median Difference (ASE) [4]	-0.65 (23.822)	
				95% CI for Median Difference [4]	-89.52, 3.21	
				p-value (Mann-Whitney U test)	0.9512	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.80	
				95% CI for SMD (Hedges' g)	-0.32, 1.92	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

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Summary of Z-scores from 9-Hole Pegboard Test by region

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	Non-US	Week 24	Absolute value	n (%)	9 (69.23)	5 (100.00)
				Number of patients with missing data: n (%)	4 (30.77)	0 (0.00)
				Mean (SD)	3.67 (2.975)	5.23 (4.749)
				Median (MAD)	3.65 (2.270)	2.12 (0.540)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

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Summary of Z-scores from 9-Hole Pegboard Test by region

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	Non-US	Week 24	Change from Baseline	n (%)	9 (69.23)	5 (100.00)
				Number of patients with missing data: n (%)	4 (30.77)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	-6.29 (1.20)	-4.51 (1.73)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.78 (2.19)	
				95% CI for LS Mean Difference [2]	-6.48, 2.92	
				p-value MMRM [2]	0.4295	
				Mean (SD)	0.58 (2.010)	-18.09 (41.702)
				Median (MAD)	0.41 (0.760)	0.70 (0.880)
				Mean Difference (SE) [3]	18.66 (13.461)	
				95% CI for Mean Difference [3]	-33.10, 70.42	
				p-value (Welch's t-test) [3]	0.3738	
				Median Difference (ASE) [4]	-0.30 (23.960)	
				95% CI for Median Difference [4]	-92.02, 1.37	
				p-value (Mann-Whitney U test)	0.7897	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.77	
				95% CI for SMD (Hedges' g)	-0.36, 1.91	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

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Summary of Z-scores from 9-Hole Pegboard Test by region

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.1715	
	US	Baseline	Absolute value	n (%)	6 (75.00)	6 (100.00)
				Number of patients with missing data: n (%)	2 (25.00)	0 (0.00)
				Mean (SD)	4.02 (5.001)	3.93 (2.387)
				Median (MAD)	2.07 (1.325)	4.97 (0.855)
		Week 12	Absolute value	n (%)	6 (75.00)	6 (100.00)
				Number of patients with missing data: n (%)	2 (25.00)	0 (0.00)
				Mean (SD)	7.51 (11.468)	3.74 (2.330)
				Median (MAD)	3.22 (2.260)	4.25 (1.680)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
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Summary of Z-scores from 9-Hole Pegboard Test by region

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	US	Week 12	Change from Baseline	n (%)	6 (75.00)	6 (100.00)
				Number of patients with missing data: n (%)	2 (25.00)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	3.48 (1.89)	-0.18 (1.89)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.66 (2.67)	
				95% CI for LS Mean Difference [2]	-2.80, 10.12	
				p-value MMRM [2]	0.2177	
				Mean (SD)	3.49 (7.037)	-0.19 (1.337)
				Median (MAD)	1.41 (3.190)	-0.48 (0.945)
				Mean Difference (SE) [3]	3.68 (2.924)	
				95% CI for Mean Difference [3]	-3.69, 11.04	
				p-value (Welch's t-test) [3]	0.2607	
				Median Difference (ASE) [4]	1.89 (4.605)	
				95% CI for Median Difference [4]	-1.65, 15.15	
				p-value (Mann-Whitney U test)	0.4712	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.73	
				95% CI for SMD (Hedges' g)	-0.45, 1.90	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

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Summary of Z-scores from 9-Hole Pegboard Test by region

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	US	Week 24	Absolute value	n (%)	6 (75.00)	6 (100.00)
				Number of patients with missing data: n (%)	2 (25.00)	0 (0.00)
				Mean (SD)	6.40 (5.513)	4.50 (3.075)
				Median (MAD)	5.01 (3.500)	3.77 (1.840)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
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Summary of Z-scores from 9-Hole Pegboard Test by region

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	US	Week 24	Change from Baseline	n (%)	6 (75.00)	6 (100.00)
				Number of patients with missing data: n (%)	2 (25.00)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	2.37 (1.42)	0.58 (1.42)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.79 (2.01)	
				95% CI for LS Mean Difference [2]	-3.06, 6.63	
				p-value MMRM [2]	0.4056	
				Mean (SD)	2.38 (3.579)	0.57 (2.505)
				Median (MAD)	1.80 (1.540)	0.40 (2.200)
				Mean Difference (SE) [3]	1.81 (1.783)	
				95% CI for Mean Difference [3]	-2.23, 5.84	
				p-value (Welch's t-test) [3]	0.3381	
				Median Difference (ASE) [4]	1.18 (2.321)	
				95% CI for Median Difference [4]	-2.40, 5.37	
				p-value (Mann-Whitney U test)	0.3785	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.58	
				95% CI for SMD (Hedges' g)	-0.58, 1.74	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

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Summary of Z-scores from 9-Hole Pegboard Test by region

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	Non-US	Baseline	Absolute value	n (%)	12 (92.31)	5 (100.00)
				Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
				Mean (SD)	2.61 (2.708)	32.48 (52.365)
				Median (MAD)	3.41 (2.750)	16.03 (13.500)
		Week 12	Absolute value	n (%)	9 (69.23)	4 (80.00)
				Number of patients with missing data: n (%)	4 (30.77)	1 (20.00)
				Mean (SD)	4.89 (5.309)	8.12 (10.459)
				Median (MAD)	3.57 (2.830)	4.39 (2.400)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

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Summary of Z-scores from 9-Hole Pegboard Test by region

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	Non-US	Week 12	Change from Baseline	n (%)	9 (69.23)	4 (80.00)
				Number of patients with missing data: n (%)	4 (30.77)	1 (20.00)
				LS Mean Change from Baseline (SE) [2]	-9.40 (2.17)	-2.84 (3.28)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-6.56 (4.11)	
				95% CI for LS Mean Difference [2]	-15.34, 2.22	
				p-value MMRM [2]	0.1320	
				Mean (SD)	2.42 (5.177)	-28.47 (61.951)
				Median (MAD)	0.51 (1.410)	1.22 (3.630)
				Mean Difference (SE) [3]	30.90 (19.622)	
				95% CI for Mean Difference [3]	-67.49, 129.28	
				p-value (Welch's t-test) [3]	0.3923	
				Median Difference (ASE) [4]	-2.36 (32.281)	
				95% CI for Median Difference [4]	-121.77, 4.77	
				p-value (Mann-Whitney U test)	0.9385	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.95	
				95% CI for SMD (Hedges' g)	-0.30, 2.19	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

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Summary of Z-scores from 9-Hole Pegboard Test by region

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	Non-US	Week 24	Absolute value	n (%)	9 (69.23)	5 (100.00)
				Number of patients with missing data: n (%)	4 (30.77)	0 (0.00)
				Mean (SD)	4.00 (3.673)	8.05 (8.220)
				Median (MAD)	3.37 (2.640)	4.50 (3.860)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
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[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
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Summary of Z-scores from 9-Hole Pegboard Test by region

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	Non-US	Week 24	Change from Baseline	n (%)	9 (69.23)	5 (100.00)
				Number of patients with missing data: n (%)	4 (30.77)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	-9.27 (1.92)	-4.03 (2.88)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-5.23 (3.66)	
				95% CI for LS Mean Difference [2]	-13.20, 2.74	
				p-value MMRM [2]	0.1783	
				Mean (SD)	0.91 (2.548)	-24.43 (55.937)
				Median (MAD)	0.07 (1.640)	1.81 (0.340)
				Mean Difference (SE) [3]	25.35 (18.051)	
				95% CI for Mean Difference [3]	-44.08, 94.78	
				p-value (Welch's t-test) [3]	0.3684	
				Median Difference (ASE) [4]	-1.63 (32.284)	
				95% CI for Median Difference [4]	-123.57, 2.17	
				p-value (Mann-Whitney U test)	0.7897	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.78	
				95% CI for SMD (Hedges' g)	-0.35, 1.92	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

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4.10.13.4 Summary of Z-scores from 9-Hole Pegboard Test by GMFCS

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.2889	
	I	Baseline	Absolute value	n (%)	7 (77.78)	5 (100.00)
				Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
				Mean (SD)	0.79 (1.671)	20.31 (41.528)
				Median (MAD)	0.93 (1.250)	1.42 (0.830)
		Week 12	Absolute value	n (%)	6 (66.67)	5 (100.00)
				Number of patients with missing data: n (%)	3 (33.33)	0 (0.00)
				Mean (SD)	1.77 (1.433)	2.35 (1.652)
				Median (MAD)	1.10 (0.385)	1.81 (1.060)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

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Summary of Z-scores from 9-Hole Pegboard Test by GMFCS

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	I	Week 12	Change from Baseline	n (%)	6 (66.67)	5 (100.00)
				Number of patients with missing data: n (%)	3 (33.33)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	-8.42 (0.62)	-8.12 (0.68)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.30 (0.95)	
				95% CI for LS Mean Difference [2]	-2.46, 1.86	
				p-value MMRM [2]	0.7620	
				Mean (SD)	0.51 (1.415)	-17.96 (40.704)
				Median (MAD)	1.05 (0.650)	0.25 (0.160)
				Mean Difference (SE) [3]	18.46 (16.444)	
				95% CI for Mean Difference [3]	-32.06, 68.99	
				p-value (Welch's t-test) [3]	0.3679	
				Median Difference (ASE) [4]	-1.10 (23.845)	
				95% CI for Median Difference [4]	-91.79, 1.68	
				p-value (Mann-Whitney U test)	0.2353	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.68	
				95% CI for SMD (Hedges' g)	-0.55, 1.91	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

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Summary of Z-scores from 9-Hole Pegboard Test by GMFCS

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	I	Week 24	Absolute value	n (%)	5 (55.56)	5 (100.00)
				Number of patients with missing data: n (%)	4 (44.44)	0 (0.00)
				Mean (SD)	1.42 (1.827)	1.31 (0.798)
				Median (MAD)	0.70 (0.720)	1.56 (0.560)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
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Summary of Z-scores from 9-Hole Pegboard Test by GMFCS

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	I	Week 24	Change from Baseline	n (%)	5 (55.56)	5 (100.00)
				Number of patients with missing data: n (%)	4 (44.44)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	-8.84 (0.67)	-9.16 (0.67)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.33 (0.97)	
				95% CI for LS Mean Difference [2]	-1.92, 2.57	
				p-value MMRM [2]	0.7464	
				Mean (SD)	0.20 (1.076)	-19.00 (41.217)
				Median (MAD)	-0.35 (0.550)	-0.37 (1.110)
				Mean Difference (SE) [3]	19.20 (18.439)	
				95% CI for Mean Difference [3]	-31.97, 70.37	
				p-value (Welch's t-test) [3]	0.3565	
				Median Difference (ASE) [4]	0.94 (23.845)	
				95% CI for Median Difference [4]	-1.15, 92.32	
				p-value (Mann-Whitney U test)	0.4034	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.66	
				95% CI for SMD (Hedges' g)	-0.62, 1.94	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

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Summary of Z-scores from 9-Hole Pegboard Test by GMFCS

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	≥ II	Baseline	Absolute value	n (%)	11 (91.67)	6 (100.00)
				Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
				Mean (SD)	3.11 (2.395)	5.32 (4.183)
				Median (MAD)	3.15 (1.150)	4.09 (2.525)
		Week 12	Absolute value	n (%)	10 (83.33)	6 (100.00)
				Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
				Mean (SD)	3.33 (2.371)	5.71 (4.048)
				Median (MAD)	3.46 (1.410)	5.03 (0.975)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

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[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

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Summary of Z-scores from 9-Hole Pegboard Test by GMFCS

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	≥ II	Week 12	Change from Baseline	n (%)	10 (83.33)	6 (100.00)
				Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	-0.18 (0.83)	1.02 (1.09)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.21 (1.42)	
				95% CI for LS Mean Difference [2]	-4.25, 1.84	
				p-value MMRM [2]	0.4088	
				Mean (SD)	0.34 (2.947)	0.39 (2.768)
				Median (MAD)	-0.39 (0.910)	1.02 (1.675)
				Mean Difference (SE) [3]	0.05 (1.489)	
				95% CI for Mean Difference [3]	-3.16, 3.27	
				p-value (Welch's t-test) [3]	0.9707	
				Median Difference (ASE) [4]	0.66 (1.870)	
				95% CI for Median Difference [4]	-3.71, 3.46	
				p-value (Mann-Whitney U test)	0.7863	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.02	
				95% CI for SMD (Hedges' g)	-1.03, 0.99	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

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[3] Based on Welch's t-test

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Summary of Z-scores from 9-Hole Pegboard Test by GMFCS

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	≥ II	Week 24	Absolute value	n (%)	10 (83.33)	6 (100.00)
				Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
				Mean (SD)	4.77 (3.567)	6.53 (3.682)
				Median (MAD)	3.97 (2.075)	6.49 (2.325)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
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[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
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Summary of Z-scores from 9-Hole Pegboard Test by GMFCS

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	≥ II	Week 24	Change from Baseline	n (%)	10 (83.33)	6 (100.00)
				Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	1.39 (1.08)	1.85 (1.43)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.46 (1.82)	
				95% CI for LS Mean Difference [2]	-4.36, 3.44	
				p-value MMRM [2]	0.8037	
				Mean (SD)	1.43 (4.512)	1.21 (1.456)
				Median (MAD)	0.20 (1.430)	1.15 (0.810)
				Mean Difference (SE) [3]	-0.22 (1.922)	
				95% CI for Mean Difference [3]	-3.60, 3.16	
				p-value (Welch's t-test) [3]	0.8896	
				Median Difference (ASE) [4]	0.94 (1.663)	
				95% CI for Median Difference [4]	-2.97, 3.09	
				p-value (Mann-Whitney U test)	0.5508	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.06	
				95% CI for SMD (Hedges' g)	-0.95, 1.07	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

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[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

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Summary of Z-scores from 9-Hole Pegboard Test by GMFCS

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.5338	
	I	Baseline	Absolute value	n (%)	7 (77.78)	5 (100.00)
				Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
				Mean (SD)	3.25 (5.117)	27.09 (54.794)
				Median (MAD)	2.85 (3.200)	2.53 (2.410)
		Week 12	Absolute value	n (%)	6 (66.67)	5 (100.00)
				Number of patients with missing data: n (%)	3 (33.33)	0 (0.00)
				Mean (SD)	6.79 (11.800)	2.02 (1.747)
				Median (MAD)	2.88 (1.930)	1.15 (0.950)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

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[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

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Summary of Z-scores from 9-Hole Pegboard Test by GMFCS

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	I	Week 12	Change from Baseline	n (%)	6 (66.67)	5 (100.00)
				Number of patients with missing data: n (%)	3 (33.33)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	-8.68 (3.84)	-12.37 (4.21)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.68 (5.72)	
				95% CI for LS Mean Difference [2]	-9.28, 16.64	
				p-value MMRM [2]	0.5361	
				Mean (SD)	2.90 (7.001)	-25.08 (53.784)
				Median (MAD)	0.76 (0.960)	-1.91 (1.000)
				Mean Difference (SE) [3]	27.98 (21.941)	
				95% CI for Mean Difference [3]	-38.55, 94.51	
				p-value (Welch's t-test) [3]	0.3107	
				Median Difference (ASE) [4]	-2.67 (31.207)	
				95% CI for Median Difference [4]	-121.43, 0.90	
				p-value (Mann-Whitney U test)	0.1207	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.77	
				95% CI for SMD (Hedges' g)	-0.47, 2.01	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

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[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

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Summary of Z-scores from 9-Hole Pegboard Test by GMFCS

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	I	Week 24	Absolute value	n (%)	5 (55.56)	5 (100.00)
				Number of patients with missing data: n (%)	4 (44.44)	0 (0.00)
				Mean (SD)	4.32 (6.418)	2.57 (1.828)
				Median (MAD)	2.44 (1.960)	2.78 (1.720)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
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Summary of Z-scores from 9-Hole Pegboard Test by GMFCS

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	I	Week 24	Change from Baseline	n (%)	5 (55.56)	5 (100.00)
				Number of patients with missing data: n (%)	4 (44.44)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	-11.76 (2.06)	-11.82 (2.23)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.06 (3.08)	
				95% CI for LS Mean Difference [2]	-6.94, 7.06	
				p-value MMRM [2]	0.9851	
				Mean (SD)	0.37 (1.200)	-24.53 (55.864)
				Median (MAD)	-0.20 (0.630)	-1.12 (3.090)
				Mean Difference (SE) [3]	24.89 (24.989)	
				95% CI for Mean Difference [3]	-44.46, 94.25	
				p-value (Welch's t-test) [3]	0.3755	
				Median Difference (ASE) [4]	0.91 (32.414)	
				95% CI for Median Difference [4]	-2.86, 124.20	
				p-value (Mann-Whitney U test)	0.6761	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.63	
				95% CI for SMD (Hedges' g)	-0.65, 1.91	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

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[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

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Summary of Z-scores from 9-Hole Pegboard Test by GMFCS

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	≥ II	Baseline	Absolute value	n (%)	11 (91.67)	6 (100.00)
				Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
				Mean (SD)	2.97 (2.372)	8.42 (7.205)
				Median (MAD)	3.30 (2.130)	5.57 (3.185)
		Week 12	Absolute value	n (%)	9 (75.00)	5 (83.33)
				Number of patients with missing data: n (%)	3 (25.00)	1 (16.67)
				Mean (SD)	5.36 (5.053)	8.97 (8.190)
				Median (MAD)	3.57 (2.730)	5.00 (0.510)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

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Summary of Z-scores from 9-Hole Pegboard Test by GMFCS

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	≥ II	Week 12	Change from Baseline	n (%)	9 (75.00)	5 (83.33)
				Number of patients with missing data: n (%)	3 (25.00)	1 (16.67)
				LS Mean Change from Baseline (SE) [2]	1.42 (1.60)	2.20 (2.24)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.79 (2.88)	
				95% CI for LS Mean Difference [2]	-6.96, 5.38	
				p-value MMRM [2]	0.7887	
				Mean (SD)	2.81 (5.256)	2.07 (2.702)
				Median (MAD)	1.47 (2.620)	1.65 (2.590)
				Mean Difference (SE) [3]	-0.74 (2.547)	
				95% CI for Mean Difference [3]	-5.38, 3.90	
				p-value (Welch's t-test) [3]	0.7336	
				Median Difference (ASE) [4]	0.18 (2.449)	
				95% CI for Median Difference [4]	-5.03, 4.26	
				p-value (Mann-Whitney U test)	1.0000	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.16	
				95% CI for SMD (Hedges' g)	-0.93, 1.26	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

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Summary of Z-scores from 9-Hole Pegboard Test by GMFCS

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	≥ II	Week 24	Absolute value	n (%)	10 (83.33)	6 (100.00)
				Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
				Mean (SD)	5.28 (3.540)	9.07 (6.680)
				Median (MAD)	5.20 (2.860)	7.98 (4.485)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
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Summary of Z-scores from 9-Hole Pegboard Test by GMFCS

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	≥ II	Week 24	Change from Baseline	n (%)	10 (83.33)	6 (100.00)
				Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	2.44 (1.25)	1.62 (1.80)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.82 (2.33)	
				95% CI for LS Mean Difference [2]	-4.50, 6.14	
				p-value MMRM [2]	0.7337	
				Mean (SD)	2.07 (3.470)	0.65 (2.865)
				Median (MAD)	1.97 (1.945)	1.87 (1.090)
				Mean Difference (SE) [3]	-1.42 (1.687)	
				95% CI for Mean Difference [3]	-4.90, 2.07	
				p-value (Welch's t-test) [3]	0.3944	
				Median Difference (ASE) [4]	-0.80 (2.038)	
				95% CI for Median Difference [4]	-5.41, 2.08	
				p-value (Mann-Whitney U test)	0.4808	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.43	
				95% CI for SMD (Hedges' g)	-0.59, 1.46	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

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4.10.13.5 Summary of Z-scores from 9-Hole Pegboard Test by gender (excluding subjects with data entry errors)

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.4040	
	Male	Baseline	Absolute value	n (%)	10 (83.33)	6 (85.71)
				Number of patients with missing data: n (%)	2 (16.67)	1 (14.29)
				Mean (SD)	2.22 (2.989)	3.60 (3.346)
				Median (MAD)	1.99 (1.660)	3.42 (1.815)
		Week 12	Absolute value	n (%)	9 (75.00)	6 (85.71)
				Number of patients with missing data: n (%)	3 (25.00)	1 (14.29)
				Mean (SD)	2.97 (2.066)	3.56 (1.823)
				Median (MAD)	2.40 (1.600)	4.10 (1.000)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: subjects excluded due to known data entry errors.

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Summary of Z-scores from 9-Hole Pegboard Test by gender (excluding subjects with data entry errors)

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	Male	Week 12	Change from Baseline	n (%)	9 (75.00)	6 (85.71)
				Number of patients with missing data: n (%)	3 (25.00)	1 (14.29)
				LS Mean Change from Baseline (SE) [2]	0.02 (0.56)	0.26 (0.68)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.25 (0.89)	
				95% CI for LS Mean Difference [2]	-2.17, 1.68	
				p-value MMRM [2]	0.7866	
				Mean (SD)	0.27 (2.301)	-0.03 (2.576)
				Median (MAD)	-0.70 (0.650)	0.32 (1.110)
				Mean Difference (SE) [3]	0.30 (1.270)	
				95% CI for Mean Difference [3]	-2.60, 3.20	
				p-value (Welch's t-test) [3]	0.8214	
				Median Difference (ASE) [4]	0.41 (1.571)	
				95% CI for Median Difference [4]	-3.21, 2.13	
				p-value (Mann-Whitney U test)	0.7683	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.13	
				95% CI for SMD (Hedges' g)	-0.91, 1.16	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: subjects excluded due to known data entry errors.

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Summary of Z-scores from 9-Hole Pegboard Test by gender (excluding subjects with data entry errors)

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	Male	Week 24	Absolute value	n (%)	8 (66.67)	6 (85.71)
				Number of patients with missing data: n (%)	4 (33.33)	1 (14.29)
				Mean (SD)	4.52 (4.318)	4.81 (3.044)
				Median (MAD)	3.03 (3.020)	4.56 (2.990)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
NOTE: subjects excluded due to known data entry errors.
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Summary of Z-scores from 9-Hole Pegboard Test by gender (excluding subjects with data entry errors)

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	Male	Week 24	Change from Baseline	n (%)	8 (66.67)	6 (85.71)
				Number of patients with missing data: n (%)	4 (33.33)	1 (14.29)
				LS Mean Change from Baseline (SE) [2]	1.29 (1.26)	1.51 (1.46)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.22 (1.93)	
				95% CI for LS Mean Difference [2]	-4.43, 3.98	
				p-value MMRM [2]	0.9102	
				Mean (SD)	1.67 (4.892)	1.22 (1.455)
				Median (MAD)	-0.38 (0.700)	1.16 (0.810)
				Mean Difference (SE) [3]	0.46 (2.081)	
				95% CI for Mean Difference [3]	-3.71, 4.62	
				p-value (Welch's t-test) [3]	0.8089	
				Median Difference (ASE) [4]	1.12 (1.985)	
				95% CI for Median Difference [4]	-4.26, 2.95	
				p-value (Mann-Whitney U test)	0.4014	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.12	
				95% CI for SMD (Hedges' g)	-0.94, 1.18	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: subjects excluded due to known data entry errors.

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Summary of Z-scores from 9-Hole Pegboard Test by gender (excluding subjects with data entry errors)

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	Female	Baseline	Absolute value	n (%)	8 (88.89)	3 (75.00)
				Number of patients with missing data: n (%)	1 (11.11)	1 (25.00)
				Mean (SD)	2.20 (1.552)	5.57 (5.013)
				Median (MAD)	2.68 (1.235)	4.15 (2.730)
		Week 12	Absolute value	n (%)	7 (77.78)	3 (75.00)
				Number of patients with missing data: n (%)	2 (22.22)	1 (25.00)
				Mean (SD)	2.46 (2.408)	6.60 (6.196)
				Median (MAD)	2.16 (2.040)	4.40 (2.590)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Subjects excluded due to known data entry errors.

Table Generation: 11SEP2023 1:00:45 PM

Program: t-qs-cont-peg9-sub.sas

Summary of Z-scores from 9-Hole Pegboard Test by gender (excluding subjects with data entry errors)

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	Female	Week 12	Change from Baseline	n (%)	7 (77.78)	3 (75.00)
				Number of patients with missing data: n (%)	2 (22.22)	1 (25.00)
				LS Mean Change from Baseline (SE) [2]	0.40 (0.95)	1.18 (1.63)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.78 (2.01)	
				95% CI for LS Mean Difference [2]	-5.36, 3.80	
				p-value MMRM [2]	0.7072	
				Mean (SD)	0.56 (2.756)	1.03 (1.238)
				Median (MAD)	1.02 (1.180)	0.39 (0.140)
				Mean Difference (SE) [3]	-0.47 (1.701)	
				95% CI for Mean Difference [3]	-3.40, 2.46	
				p-value (Welch's t-test) [3]	0.7203	
				Median Difference (ASE) [4]	0.41 (2.839)	
				95% CI for Median Difference [4]	-4.07, 4.85	
				p-value (Mann-Whitney U test)	0.8197	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.19	
				95% CI for SMD (Hedges' g)	-1.55, 1.17	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Subjects excluded due to known data entry errors.

Table Generation: 11SEP2023 1:00:45 PM

Program: t-qs-cont-peg9-sub.sas

Summary of Z-scores from 9-Hole Pegboard Test by gender (excluding subjects with data entry errors)

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	Female	Week 24	Absolute value	n (%)	7 (77.78)	3 (75.00)
				Number of patients with missing data: n (%)	2 (22.22)	1 (25.00)
				Mean (SD)	2.67 (1.914)	4.91 (6.058)
				Median (MAD)	2.50 (1.800)	2.12 (1.370)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
NOTE: Subjects excluded due to known data entry errors.
Table Generation: 11SEP2023 1:00:45 PM
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Summary of Z-scores from 9-Hole Pegboard Test by gender (excluding subjects with data entry errors)

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	Female	Week 24	Change from Baseline	n (%)	7 (77.78)	3 (75.00)
				Number of patients with missing data: n (%)	2 (22.22)	1 (25.00)
				LS Mean Change from Baseline (SE) [2]	0.69 (0.88)	-0.51 (1.53)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.20 (1.89)	
				95% CI for LS Mean Difference [2]	-3.29, 5.69	
				p-value MMRM [2]	0.5456	
				Mean (SD)	0.28 (1.739)	-0.66 (2.373)
				Median (MAD)	0.41 (0.610)	0.70 (0.020)
				Mean Difference (SE) [3]	0.94 (1.323)	
				95% CI for Mean Difference [3]	-3.92, 5.80	
				p-value (Welch's t-test) [3]	0.5814	
				Median Difference (ASE) [4]	-0.32 (2.416)	
				95% CI for Median Difference [4]	-5.04, 3.84	
				p-value (Mann-Whitney U test)	0.6485	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.49	
				95% CI for SMD (Hedges' g)	-0.88, 1.86	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Subjects excluded due to known data entry errors.

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Summary of Z-scores from 9-Hole Pegboard Test by gender (excluding subjects with data entry errors)

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.3468	
	Male	Baseline	Absolute value	n (%)	10 (83.33)	6 (85.71)
				Number of patients with missing data: n (%)	2 (16.67)	1 (14.29)
				Mean (SD)	3.71 (4.203)	5.64 (5.526)
				Median (MAD)	3.41 (1.395)	4.97 (1.935)
		Week 12	Absolute value	n (%)	8 (66.67)	5 (71.43)
				Number of patients with missing data: n (%)	4 (33.33)	2 (28.57)
				Mean (SD)	7.72 (9.834)	4.46 (2.200)
				Median (MAD)	5.25 (3.415)	4.80 (0.310)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
NOTE: Subjects excluded due to known data entry errors.
Table Generation: 11SEP2023 1:00:45 PM
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Summary of Z-scores from 9-Hole Pegboard Test by gender (excluding subjects with data entry errors)

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	Male	Week 12	Change from Baseline	n (%)	8 (66.67)	5 (71.43)
				Number of patients with missing data: n (%)	4 (33.33)	2 (28.57)
				LS Mean Change from Baseline (SE) [2]	3.35 (1.84)	0.70 (2.33)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.65 (2.97)	
				95% CI for LS Mean Difference [2]	-4.09, 9.39	
				p-value MMRM [2]	0.3960	
				Mean (SD)	3.43 (5.952)	0.90 (2.403)
				Median (MAD)	2.00 (2.015)	-0.05 (0.890)
				Mean Difference (SE) [3]	2.52 (2.830)	
				95% CI for Mean Difference [3]	-2.74, 7.79	
				p-value (Welch's t-test) [3]	0.3106	
				Median Difference (ASE) [4]	-1.10 (2.253)	
				95% CI for Median Difference [4]	-6.04, 2.12	
				p-value (Mann-Whitney U test)	0.3413	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.51	
				95% CI for SMD (Hedges' g)	-0.63, 1.65	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Subjects excluded due to known data entry errors.

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Summary of Z-scores from 9-Hole Pegboard Test by gender (excluding subjects with data entry errors)

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	Male	Week 24	Absolute value	n (%)	8 (66.67)	6 (85.71)
				Number of patients with missing data: n (%)	4 (33.33)	1 (14.29)
				Mean (SD)	6.75 (5.265)	5.80 (4.470)
				Median (MAD)	8.00 (3.465)	4.91 (3.345)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
NOTE: Subjects excluded due to known data entry errors.
Table Generation: 11SEP2023 1:00:45 PM
Program: t-qs-cont-peg9-sub.sas

Summary of Z-scores from 9-Hole Pegboard Test by gender (excluding subjects with data entry errors)

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	Male	Week 24	Change from Baseline	n (%)	8 (66.67)	6 (85.71)
				Number of patients with missing data: n (%)	4 (33.33)	1 (14.29)
				LS Mean Change from Baseline (SE) [2]	2.41 (1.16)	0.22 (1.34)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.19 (1.78)	
				95% CI for LS Mean Difference [2]	-1.78, 6.16	
				p-value MMRM [2]	0.2471	
				Mean (SD)	2.50 (3.381)	0.16 (2.877)
				Median (MAD)	1.54 (2.095)	0.40 (2.095)
				Mean Difference (SE) [3]	2.33 (1.718)	
				95% CI for Mean Difference [3]	-1.33, 5.99	
				p-value (Welch's t-test) [3]	0.1897	
				Median Difference (ASE) [4]	-1.99 (2.375)	
				95% CI for Median Difference [4]	-6.27, 2.08	
				p-value (Mann-Whitney U test)	0.2725	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.73	
				95% CI for SMD (Hedges' g)	-0.36, 1.83	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Subjects excluded due to known data entry errors.

Table Generation: 11SEP2023 1:00:45 PM

Program: t-qs-cont-peg9-sub.sas

Summary of Z-scores from 9-Hole Pegboard Test by gender (excluding subjects with data entry errors)

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	Female	Baseline	Absolute value	n (%)	8 (88.89)	3 (75.00)
				Number of patients with missing data: n (%)	1 (11.11)	1 (25.00)
				Mean (SD)	2.29 (2.558)	9.01 (8.461)
				Median (MAD)	1.02 (1.035)	5.91 (3.380)
		Week 12	Absolute value	n (%)	7 (77.78)	3 (75.00)
				Number of patients with missing data: n (%)	2 (22.22)	1 (25.00)
				Mean (SD)	3.89 (5.420)	9.24 (12.506)
				Median (MAD)	1.78 (0.520)	4.00 (3.800)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Subjects excluded due to known data entry errors.

Table Generation: 11SEP2023 1:00:45 PM

Program: t-qs-cont-peg9-sub.sas

Summary of Z-scores from 9-Hole Pegboard Test by gender (excluding subjects with data entry errors)

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	Female	Week 12	Change from Baseline	n (%)	7 (77.78)	3 (75.00)
				Number of patients with missing data: n (%)	2 (22.22)	1 (25.00)
				LS Mean Change from Baseline (SE) [2]	0.88 (2.23)	1.04 (3.69)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.16 (4.41)	
				95% CI for LS Mean Difference [2]	-10.07, 9.75	
				p-value MMRM [2]	0.9720	
				Mean (SD)	2.19 (5.950)	0.23 (4.076)
				Median (MAD)	0.51 (1.410)	-1.91 (0.420)
				Mean Difference (SE) [3]	1.96 (3.824)	
				95% CI for Mean Difference [3]	-6.10, 10.01	
				p-value (Welch's t-test) [3]	0.5706	
				Median Difference (ASE) [4]	-1.91 (6.388)	
				95% CI for Median Difference [4]	-17.13, 6.18	
				p-value (Mann-Whitney U test)	0.6485	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.35	
				95% CI for SMD (Hedges' g)	-1.01, 1.72	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Subjects excluded due to known data entry errors.

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Summary of Z-scores from 9-Hole Pegboard Test by gender (excluding subjects with data entry errors)

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	Female	Week 24	Absolute value	n (%)	7 (77.78)	3 (75.00)
				Number of patients with missing data: n (%)	2 (22.22)	1 (25.00)
				Mean (SD)	2.90 (2.282)	9.69 (9.271)
				Median (MAD)	2.98 (1.420)	4.50 (0.330)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
NOTE: Subjects excluded due to known data entry errors.
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Summary of Z-scores from 9-Hole Pegboard Test by gender (excluding subjects with data entry errors)

Hand Dominance	Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	Female	Week 24	Change from Baseline	n (%)	7 (77.78)	3 (75.00)
				Number of patients with missing data: n (%)	2 (22.22)	1 (25.00)
				LS Mean Change from Baseline (SE) [2]	0.94 (1.24)	1.49 (2.18)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.55 (2.71)	
				95% CI for LS Mean Difference [2]	-8.39, 7.29	
				p-value MMRM [2]	0.8505	
				Mean (SD)	0.36 (2.110)	0.68 (2.097)
				Median (MAD)	-0.02 (1.940)	1.81 (0.160)
				Mean Difference (SE) [3]	-0.32 (1.454)	
				95% CI for Mean Difference [3]	-4.40, 3.76	
				p-value (Welch's t-test) [3]	0.8372	
				Median Difference (ASE) [4]	-0.11 (2.485)	
				95% CI for Median Difference [4]	-3.97, 5.17	
				p-value (Mann-Whitney U test)	1.0000	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.15	
				95% CI for SMD (Hedges' g)	-1.51, 1.20	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Subjects excluded due to known data entry errors.

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4.10.13.6 Summary of Z-scores from 9-Hole Pegboard Test by age group (excluding subjects with data entry errors)

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.0160 ***	
	<10.5 years old at screening	Baseline	Absolute value	n (%)	9 (75.00)	3 (75.00)
				Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
				Mean (SD)	1.71 (1.977)	6.44 (4.090)
				Median (MAD)	2.68 (0.970)	4.45 (0.730)
		Week 12	Absolute value	n (%)	8 (66.67)	3 (75.00)
				Number of patients with missing data: n (%)	4 (33.33)	1 (25.00)
				Mean (SD)	1.92 (1.753)	7.93 (4.908)
				Median (MAD)	2.28 (0.995)	5.15 (0.100)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Median age used as cut-off point.

NOTE: Subjects excluded due to known data entry errors.

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Table Generation: 11SEP2023 1:00:53 PM

Summary of Z-scores from 9-Hole Pegboard Test by age group (excluding subjects with data entry errors)

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	<10.5 years old at screening	Week 12	Change from Baseline	n (%)	8 (66.67)	3 (75.00)
				Number of patients with missing data: n (%)	4 (33.33)	1 (25.00)
				LS Mean Change from Baseline (SE) [2]	-0.36 (0.76)	1.74 (1.41)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-2.11 (1.76)	
				95% CI for LS Mean Difference [2]	-6.08, 1.87	
				p-value MMRM [2]	0.2622	
				Mean (SD)	-0.27 (2.092)	1.50 (0.892)
				Median (MAD)	-0.34 (1.135)	1.33 (0.630)
				Mean Difference (SE) [3]	1.77 (1.281)	
				95% CI for Mean Difference [3]	-0.29, 3.82	
				p-value (Welch's t-test) [3]	0.0836	
				Median Difference (ASE) [4]	1.47 (1.776)	
				95% CI for Median Difference [4]	-0.76, 5.16	
				p-value (Mann-Whitney U test)	0.1846	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.93	
				95% CI for SMD (Hedges' g)	-2.33, 0.46	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Median age used as cut-off point.

NOTE: Subjects excluded due to known data entry errors.

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Summary of Z-scores from 9-Hole Pegboard Test by age group (excluding subjects with data entry errors)

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	<10.5 years old at screening	Week 24	Absolute value	n (%)	8 (66.67)	3 (75.00)
				Number of patients with missing data: n (%)	4 (33.33)	1 (25.00)
				Mean (SD)	2.80 (2.933)	7.94 (3.905)
				Median (MAD)	1.94 (1.630)	7.90 (3.850)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
NOTE: Median age used as cut-off point.
NOTE: Subjects excluded due to known data entry errors.
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Table Generation: 11SEP2023 1:00:53 PM

Summary of Z-scores from 9-Hole Pegboard Test by age group (excluding subjects with data entry errors)

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	<10.5 years old at screening	Week 24	Change from Baseline	n (%)	8 (66.67)	3 (75.00)
				Number of patients with missing data: n (%)	4 (33.33)	1 (25.00)
				LS Mean Change from Baseline (SE) [2]	0.52 (0.87)	1.75 (1.58)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.22 (1.94)	
				95% CI for LS Mean Difference [2]	-5.54, 3.09	
				p-value MMRM [2]	0.5427	
				Mean (SD)	0.62 (2.361)	1.50 (1.700)
				Median (MAD)	0.46 (0.995)	0.72 (0.390)
				Mean Difference (SE) [3]	0.88 (1.510)	
				95% CI for Mean Difference [3]	-2.40, 4.17	
				p-value (Welch's t-test) [3]	0.5218	
				Median Difference (ASE) [4]	0.70 (2.202)	
				95% CI for Median Difference [4]	-1.88, 3.86	
				p-value (Mann-Whitney U test)	0.6098	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.40	
				95% CI for SMD (Hedges' g)	-1.74, 0.94	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Median age used as cut-off point.

NOTE: Subjects excluded due to known data entry errors.

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Summary of Z-scores from 9-Hole Pegboard Test by age group (excluding subjects with data entry errors)

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	9 (100.00)	6 (85.71)
				Number of patients with missing data: n (%)	0 (0.00)	1 (14.29)
				Mean (SD)	2.71 (2.773)	3.16 (3.440)
				Median (MAD)	2.48 (1.820)	2.27 (1.665)
		Week 12	Absolute value	n (%)	8 (88.89)	6 (85.71)
				Number of patients with missing data: n (%)	1 (11.11)	1 (14.29)
				Mean (SD)	3.57 (2.313)	2.90 (1.613)
				Median (MAD)	4.36 (1.770)	2.72 (1.295)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Median age used as cut-off point.

NOTE: Subjects excluded due to known data entry errors.

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Summary of Z-scores from 9-Hole Pegboard Test by age group (excluding subjects with data entry errors)

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	≥ 10.5 years old at screening	Week 12	Change from Baseline	n (%)	8 (88.89)	6 (85.71)
				Number of patients with missing data: n (%)	1 (11.11)	1 (14.29)
				LS Mean Change from Baseline (SE) [2]	0.75 (0.62)	-0.14 (0.71)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.89 (0.94)	
				95% CI for LS Mean Difference [2]	-1.17, 2.95	
				p-value MMRM [2]	0.3655	
				Mean (SD)	1.07 (2.685)	-0.26 (2.479)
				Median (MAD)	0.41 (1.435)	0.09 (0.640)
				Mean Difference (SE) [3]	1.33 (1.405)	
				95% CI for Mean Difference [3]	-1.71, 4.37	
				p-value (Welch's t-test) [3]	0.3575	
				Median Difference (ASE) [4]	-0.98 (1.796)	
				95% CI for Median Difference [4]	-5.16, 1.68	
				p-value (Mann-Whitney U test)	0.6514	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.51	
				95% CI for SMD (Hedges' g)	-0.57, 1.59	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Median age used as cut-off point.

NOTE: Subjects excluded due to known data entry errors.

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Summary of Z-scores from 9-Hole Pegboard Test by age group (excluding subjects with data entry errors)

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	7 (77.78)	6 (85.71)
				Number of patients with missing data: n (%)	2 (22.22)	1 (14.29)
				Mean (SD)	4.63 (3.927)	3.30 (3.039)
				Median (MAD)	4.28 (2.210)	1.85 (0.695)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
NOTE: Median age used as cut-off point.
NOTE: Subjects excluded due to known data entry errors.
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Summary of Z-scores from 9-Hole Pegboard Test by age group (excluding subjects with data entry errors)

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	≥ 10.5 years old at screening	Week 24	Change from Baseline	n (%)	7 (77.78)	6 (85.71)
				Number of patients with missing data: n (%)	2 (22.22)	1 (14.29)
				LS Mean Change from Baseline (SE) [2]	1.60 (1.29)	0.26 (1.42)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.34 (1.92)	
				95% CI for LS Mean Difference [2]	-2.91, 5.58	
				p-value MMRM [2]	0.5020	
				Mean (SD)	1.48 (5.018)	0.13 (1.968)
				Median (MAD)	-0.35 (0.330)	0.72 (1.045)
				Mean Difference (SE) [3]	1.35 (2.190)	
				95% CI for Mean Difference [3]	-3.40, 6.10	
				p-value (Welch's t-test) [3]	0.5307	
				Median Difference (ASE) [4]	0.52 (1.872)	
				95% CI for Median Difference [4]	-5.04, 2.30	
				p-value (Mann-Whitney U test)	0.9431	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.34	
				95% CI for SMD (Hedges' g)	-0.76, 1.44	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Median age used as cut-off point.

NOTE: Subjects excluded due to known data entry errors.

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Summary of Z-scores from 9-Hole Pegboard Test by age group (excluding subjects with data entry errors)

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.4140	
	<10.5 years old at screening	Baseline	Absolute value	n (%)	9 (75.00)	3 (75.00)
				Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
				Mean (SD)	2.97 (4.432)	9.91 (7.513)
				Median (MAD)	1.28 (1.830)	5.74 (0.340)
		Week 12	Absolute value	n (%)	7 (58.33)	3 (75.00)
				Number of patients with missing data: n (%)	5 (41.67)	1 (25.00)
				Mean (SD)	5.85 (10.922)	11.79 (10.215)
				Median (MAD)	1.78 (0.520)	7.05 (2.250)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
NOTE: Median age used as cut-off point.
NOTE: Subjects excluded due to known data entry errors.
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Summary of Z-scores from 9-Hole Pegboard Test by age group (excluding subjects with data entry errors)

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	<10.5 years old at screening	Week 12	Change from Baseline	n (%)	7 (58.33)	3 (75.00)
				Number of patients with missing data: n (%)	5 (41.67)	1 (25.00)
				LS Mean Change from Baseline (SE) [2]	3.00 (1.90)	0.84 (2.92)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.16 (3.52)	
				95% CI for LS Mean Difference [2]	-6.04, 10.36	
				p-value MMRM [2]	0.5572	
				Mean (SD)	2.42 (6.525)	1.88 (2.942)
				Median (MAD)	0.51 (1.410)	1.65 (2.590)
				Mean Difference (SE) [3]	-0.54 (4.029)	
				95% CI for Mean Difference [3]	-7.48, 6.40	
				p-value (Welch's t-test) [3]	0.8611	
				Median Difference (ASE) [4]	1.14 (6.436)	
				95% CI for Median Difference [4]	-15.15, 6.18	
				p-value (Mann-Whitney U test)	0.6485	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.09	
				95% CI for SMD (Hedges' g)	-1.26, 1.45	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Median age used as cut-off point.

NOTE: Subjects excluded due to known data entry errors.

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Summary of Z-scores from 9-Hole Pegboard Test by age group (excluding subjects with data entry errors)

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	<10.5 years old at screening	Week 24	Absolute value	n (%)	8 (66.67)	3 (75.00)
				Number of patients with missing data: n (%)	4 (33.33)	1 (25.00)
				Mean (SD)	4.83 (4.880)	11.08 (8.625)
				Median (MAD)	3.18 (2.525)	9.50 (6.140)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
NOTE: Median age used as cut-off point.
NOTE: Subjects excluded due to known data entry errors.
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Summary of Z-scores from 9-Hole Pegboard Test by age group (excluding subjects with data entry errors)

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	<10.5 years old at screening	Week 24	Change from Baseline	n (%)	8 (66.67)	3 (75.00)
				Number of patients with missing data: n (%)	4 (33.33)	1 (25.00)
				LS Mean Change from Baseline (SE) [2]	1.83 (0.81)	0.14 (1.39)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.69 (1.68)	
				95% CI for LS Mean Difference [2]	-2.20, 5.58	
				p-value MMRM [2]	0.3453	
				Mean (SD)	1.41 (1.534)	1.18 (2.951)
				Median (MAD)	1.64 (1.300)	1.81 (1.950)
				Mean Difference (SE) [3]	-0.24 (1.314)	
				95% CI for Mean Difference [3]	-6.78, 6.31	
				p-value (Welch's t-test) [3]	0.9053	
				Median Difference (ASE) [4]	-0.06 (2.166)	
				95% CI for Median Difference [4]	-4.27, 3.69	
				p-value (Mann-Whitney U test)	0.9187	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.12	
				95% CI for SMD (Hedges' g)	-1.21, 1.45	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Median age used as cut-off point.

NOTE: Subjects excluded due to known data entry errors.

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Summary of Z-scores from 9-Hole Pegboard Test by age group (excluding subjects with data entry errors)

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	9 (100.00)	6 (85.71)
				Number of patients with missing data: n (%)	0 (0.00)	1 (14.29)
				Mean (SD)	3.19 (2.653)	5.19 (5.677)
				Median (MAD)	3.55 (2.380)	3.54 (2.020)
		Week 12	Absolute value	n (%)	8 (88.89)	5 (71.43)
				Number of patients with missing data: n (%)	1 (11.11)	2 (28.57)
				Mean (SD)	6.01 (5.238)	2.93 (2.191)
				Median (MAD)	5.45 (3.210)	4.00 (1.000)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Median age used as cut-off point.

NOTE: Subjects excluded due to known data entry errors.

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Summary of Z-scores from 9-Hole Pegboard Test by age group (excluding subjects with data entry errors)

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	≥ 10.5 years old at screening	Week 12	Change from Baseline	n (%)	8 (88.89)	5 (71.43)
				Number of patients with missing data: n (%)	1 (11.11)	2 (28.57)
				LS Mean Change from Baseline (SE) [2]	2.37 (1.51)	-0.03 (1.89)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.40 (2.44)	
				95% CI for LS Mean Difference [2]	-2.94, 7.74	
				p-value MMRM [2]	0.3461	
				Mean (SD)	3.22 (5.455)	-0.09 (2.856)
				Median (MAD)	2.00 (2.045)	-0.91 (1.000)
				Mean Difference (SE) [3]	3.31 (2.668)	
				95% CI for Mean Difference [3]	-1.79, 8.41	
				p-value (Welch's t-test) [3]	0.1807	
				Median Difference (ASE) [4]	-2.41 (2.444)	
				95% CI for Median Difference [4]	-7.04, 1.90	
				p-value (Mann-Whitney U test)	0.1643	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.71	
				95% CI for SMD (Hedges' g)	-0.45, 1.86	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Median age used as cut-off point.

NOTE: Subjects excluded due to known data entry errors.

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Summary of Z-scores from 9-Hole Pegboard Test by age group (excluding subjects with data entry errors)

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	≥ 10.5 years old at screening	Week 24	Absolute value	n (%)	7 (77.78)	6 (85.71)
				Number of patients with missing data: n (%)	2 (22.22)	1 (14.29)
				Mean (SD)	5.11 (4.352)	5.10 (4.041)
				Median (MAD)	4.40 (4.300)	4.34 (2.040)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
NOTE: Median age used as cut-off point.
NOTE: Subjects excluded due to known data entry errors.
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Summary of Z-scores from 9-Hole Pegboard Test by age group (excluding subjects with data entry errors)

Hand Dominance	Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	≥ 10.5 years old at screening	Week 24	Change from Baseline	n (%)	7 (77.78)	6 (85.71)
				Number of patients with missing data: n (%)	2 (22.22)	1 (14.29)
				LS Mean Change from Baseline (SE) [2]	2.35 (1.64)	0.77 (1.97)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.58 (2.58)	
				95% CI for LS Mean Difference [2]	-4.56, 7.73	
				p-value MMRM [2]	0.5597	
				Mean (SD)	1.60 (4.225)	-0.09 (2.454)
				Median (MAD)	-0.20 (1.910)	0.40 (1.660)
				Mean Difference (SE) [3]	1.69 (1.965)	
				95% CI for Mean Difference [3]	-2.53, 5.90	
				p-value (Welch's t-test) [3]	0.3927	
				Median Difference (ASE) [4]	-0.92 (2.434)	
				95% CI for Median Difference [4]	-6.98, 2.56	
				p-value (Mann-Whitney U test)	0.6171	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.48	
				95% CI for SMD (Hedges' g)	-0.63, 1.59	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Median age used as cut-off point.

NOTE: Subjects excluded due to known data entry errors.

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4.10.13.7 Summary of Z-scores from 9-Hole Pegboard Test by region (excluding subjects with data entry errors)

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.6412	
	US	Baseline	Absolute value	n (%)	6 (75.00)	5 (83.33)
				Number of patients with missing data: n (%)	2 (25.00)	1 (16.67)
				Mean (SD)	1.94 (1.617)	3.25 (1.449)
				Median (MAD)	2.58 (0.630)	3.72 (0.600)
		Week 12	Absolute value	n (%)	6 (75.00)	5 (83.33)
				Number of patients with missing data: n (%)	2 (25.00)	1 (16.67)
				Mean (SD)	2.41 (2.282)	3.52 (1.944)
				Median (MAD)	2.48 (1.985)	4.40 (0.750)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Subjects excluded due to known data entry errors.

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Summary of Z-scores from 9-Hole Pegboard Test by region (excluding subjects with data entry errors)

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	US	Week 12	Change from Baseline	n (%)	6 (75.00)	5 (83.33)
				Number of patients with missing data: n (%)	2 (25.00)	1 (16.67)
				LS Mean Change from Baseline (SE) [2]	-0.13 (0.98)	0.97 (1.09)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.10 (1.55)	
				95% CI for LS Mean Difference [2]	-4.68, 2.47	
				p-value MMRM [2]	0.4973	
				Mean (SD)	0.46 (3.481)	0.26 (0.832)
				Median (MAD)	0.67 (1.920)	0.25 (0.450)
				Mean Difference (SE) [3]	0.20 (1.607)	
				95% CI for Mean Difference [3]	-3.45, 3.84	
				p-value (Welch's t-test) [3]	0.8968	
				Median Difference (ASE) [4]	-0.46 (2.357)	
				95% CI for Median Difference [4]	-4.85, 4.39	
				p-value (Mann-Whitney U test)	0.9273	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.08	
				95% CI for SMD (Hedges' g)	-1.11, 1.26	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Subjects excluded due to known data entry errors.

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Summary of Z-scores from 9-Hole Pegboard Test by region (excluding subjects with data entry errors)

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	US	Week 24	Absolute value	n (%)	6 (75.00)	5 (83.33)
				Number of patients with missing data: n (%)	2 (25.00)	1 (16.67)
				Mean (SD)	3.63 (4.346)	3.87 (2.863)
				Median (MAD)	2.29 (2.075)	4.05 (2.490)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
NOTE: Subjects excluded due to known data entry errors.
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Summary of Z-scores from 9-Hole Pegboard Test by region (excluding subjects with data entry errors)

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	US	Week 24	Change from Baseline	n (%)	6 (75.00)	5 (83.33)
				Number of patients with missing data: n (%)	2 (25.00)	1 (16.67)
				LS Mean Change from Baseline (SE) [2]	1.10 (1.60)	1.32 (1.76)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.23 (2.43)	
				95% CI for LS Mean Difference [2]	-5.73, 5.28	
				p-value MMRM [2]	0.9277	
				Mean (SD)	1.69 (5.588)	0.61 (2.551)
				Median (MAD)	-0.30 (1.555)	0.74 (1.210)
				Mean Difference (SE) [3]	1.07 (2.724)	
				95% CI for Mean Difference [3]	-4.92, 7.06	
				p-value (Welch's t-test) [3]	0.6858	
				Median Difference (ASE) [4]	0.83 (3.694)	
				95% CI for Median Difference [4]	-10.60, 3.88	
				p-value (Mann-Whitney U test)	0.7842	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.24	
				95% CI for SMD (Hedges' g)	-0.95, 1.43	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Subjects excluded due to known data entry errors.

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Summary of Z-scores from 9-Hole Pegboard Test by region (excluding subjects with data entry errors)

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	Non-US	Baseline	Absolute value	n (%)	12 (92.31)	4 (80.00)
				Number of patients with missing data: n (%)	1 (7.69)	1 (20.00)
				Mean (SD)	2.34 (2.756)	5.51 (5.609)
				Median (MAD)	2.09 (1.660)	5.44 (4.730)
		Week 12	Absolute value	n (%)	10 (76.92)	4 (80.00)
				Number of patients with missing data: n (%)	3 (23.08)	1 (20.00)
				Mean (SD)	2.95 (2.181)	5.90 (5.295)
				Median (MAD)	2.40 (1.650)	4.10 (1.595)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Subjects excluded due to known data entry errors.

Table Generation: 11SEP2023 1:01:01 PM

Program: t-qs-cont-peg9-sub.sas

Summary of Z-scores from 9-Hole Pegboard Test by region (excluding subjects with data entry errors)

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	Non-US	Week 12	Change from Baseline	n (%)	10 (76.92)	4 (80.00)
				Number of patients with missing data: n (%)	3 (23.08)	1 (20.00)
				LS Mean Change from Baseline (SE) [2]	0.15 (0.69)	0.77 (1.08)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.62 (1.31)	
				95% CI for LS Mean Difference [2]	-3.46, 2.22	
				p-value MMRM [2]	0.6414	
				Mean (SD)	0.36 (1.752)	0.40 (3.450)
				Median (MAD)	-0.21 (1.090)	1.42 (1.405)
				Mean Difference (SE) [3]	-0.04 (1.359)	
				95% CI for Mean Difference [3]	-5.27, 5.20	
				p-value (Welch's t-test) [3]	0.9846	
				Median Difference (ASE) [4]	1.12 (2.018)	
				95% CI for Median Difference [4]	-4.20, 3.71	
				p-value (Mann-Whitney U test)	0.6206	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.02	
				95% CI for SMD (Hedges' g)	-1.18, 1.14	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Subjects excluded due to known data entry errors.

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Summary of Z-scores from 9-Hole Pegboard Test by region (excluding subjects with data entry errors)

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	Non-US	Week 24	Absolute value	n (%)	9 (69.23)	4 (80.00)
				Number of patients with missing data: n (%)	4 (30.77)	1 (20.00)
				Mean (SD)	3.67 (2.975)	6.07 (5.040)
				Median (MAD)	3.65 (2.270)	5.41 (3.560)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
NOTE: Subjects excluded due to known data entry errors.
Table Generation: 11SEP2023 1:01:01 PM
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Summary of Z-scores from 9-Hole Pegboard Test by region (excluding subjects with data entry errors)

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	Non-US	Week 24	Change from Baseline	n (%)	9 (69.23)	4 (80.00)
				Number of patients with missing data: n (%)	4 (30.77)	1 (20.00)
				LS Mean Change from Baseline (SE) [2]	0.50 (0.61)	0.94 (0.93)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.44 (1.13)	
				95% CI for LS Mean Difference [2]	-2.94, 2.06	
				p-value MMRM [2]	0.7071	
				Mean (SD)	0.58 (2.010)	0.56 (0.971)
				Median (MAD)	0.41 (0.760)	0.71 (0.440)
				Mean Difference (SE) [3]	0.02 (1.074)	
				95% CI for Mean Difference [3]	-1.81, 1.84	
				p-value (Welch's t-test) [3]	0.9853	
				Median Difference (ASE) [4]	0.25 (1.105)	
				95% CI for Median Difference [4]	-2.40, 1.93	
				p-value (Mann-Whitney U test)	0.8170	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.01	
				95% CI for SMD (Hedges' g)	-1.17, 1.19	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Subjects excluded due to known data entry errors.

Table Generation: 11SEP2023 1:01:01 PM

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Summary of Z-scores from 9-Hole Pegboard Test by region (excluding subjects with data entry errors)

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.3915	
	US	Baseline	Absolute value	n (%)	6 (75.00)	5 (83.33)
				Number of patients with missing data: n (%)	2 (25.00)	1 (16.67)
				Mean (SD)	4.02 (5.001)	4.69 (1.664)
				Median (MAD)	2.07 (1.325)	5.40 (0.510)
		Week 12	Absolute value	n (%)	6 (75.00)	5 (83.33)
				Number of patients with missing data: n (%)	2 (25.00)	1 (16.67)
				Mean (SD)	7.51 (11.468)	4.26 (2.184)
				Median (MAD)	3.22 (2.260)	4.49 (0.490)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
NOTE: Subjects excluded due to known data entry errors.
Table Generation: 11SEP2023 1:01:01 PM
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Summary of Z-scores from 9-Hole Pegboard Test by region (excluding subjects with data entry errors)

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	US	Week 12	Change from Baseline	n (%)	6 (75.00)	5 (83.33)
				Number of patients with missing data: n (%)	2 (25.00)	1 (16.67)
				LS Mean Change from Baseline (SE) [2]	3.61 (1.78)	-0.58 (1.95)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	4.19 (2.65)	
				95% CI for LS Mean Difference [2]	-2.52, 10.89	
				p-value MMRM [2]	0.1718	
				Mean (SD)	3.49 (7.037)	-0.43 (1.337)
				Median (MAD)	1.41 (3.190)	-0.91 (0.860)
				Mean Difference (SE) [3]	3.92 (3.222)	
				95% CI for Mean Difference [3]	-3.45, 11.29	
				p-value (Welch's t-test) [3]	0.2348	
				Median Difference (ASE) [4]	-2.27 (4.719)	
				95% CI for Median Difference [4]	-16.85, 1.65	
				p-value (Mann-Whitney U test)	0.5228	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.74	
				95% CI for SMD (Hedges' g)	-0.50, 1.97	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Subjects excluded due to known data entry errors.

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Summary of Z-scores from 9-Hole Pegboard Test by region (excluding subjects with data entry errors)

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	US	Week 24	Absolute value	n (%)	6 (75.00)	5 (83.33)
				Number of patients with missing data: n (%)	2 (25.00)	1 (16.67)
				Mean (SD)	6.40 (5.513)	4.85 (3.306)
				Median (MAD)	5.01 (3.500)	4.17 (2.290)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
NOTE: Subjects excluded due to known data entry errors.
Table Generation: 11SEP2023 1:01:01 PM
Program: t-qs-cont-peg9-sub.sas

Summary of Z-scores from 9-Hole Pegboard Test by region (excluding subjects with data entry errors)

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	US	Week 24	Change from Baseline	n (%)	6 (75.00)	5 (83.33)
				Number of patients with missing data: n (%)	2 (25.00)	1 (16.67)
				LS Mean Change from Baseline (SE) [2]	2.50 (1.56)	0.01 (1.71)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.49 (2.32)	
				95% CI for LS Mean Difference [2]	-3.42, 8.39	
				p-value MMRM [2]	0.3314	
				Mean (SD)	2.38 (3.579)	0.16 (2.557)
				Median (MAD)	1.80 (1.540)	-1.12 (0.920)
				Mean Difference (SE) [3]	2.22 (1.917)	
				95% CI for Mean Difference [3]	-1.99, 6.43	
				p-value (Welch's t-test) [3]	0.2621	
				Median Difference (ASE) [4]	-1.48 (2.452)	
				95% CI for Median Difference [4]	-7.21, 2.40	
				p-value (Mann-Whitney U test)	0.2353	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.70	
				95% CI for SMD (Hedges' g)	-0.53, 1.93	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Subjects excluded due to known data entry errors.

Table Generation: 11SEP2023 1:01:01 PM

Program: t-qs-cont-peg9-sub.sas

Summary of Z-scores from 9-Hole Pegboard Test by region (excluding subjects with data entry errors)

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	Non-US	Baseline	Absolute value	n (%)	12 (92.31)	4 (80.00)
				Number of patients with missing data: n (%)	1 (7.69)	1 (20.00)
				Mean (SD)	2.61 (2.708)	9.34 (9.301)
				Median (MAD)	3.41 (2.750)	9.28 (7.900)
		Week 12	Absolute value	n (%)	9 (69.23)	3 (60.00)
				Number of patients with missing data: n (%)	4 (30.77)	2 (40.00)
				Mean (SD)	4.89 (5.309)	9.57 (12.309)
				Median (MAD)	3.57 (2.830)	5.00 (4.800)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Subjects excluded due to known data entry errors.

Table Generation: 11SEP2023 1:01:01 PM

Program: t-qs-cont-peg9-sub.sas

Summary of Z-scores from 9-Hole Pegboard Test by region (excluding subjects with data entry errors)

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	Non-US	Week 12	Change from Baseline	n (%)	9 (69.23)	3 (60.00)
				Number of patients with missing data: n (%)	4 (30.77)	2 (40.00)
				LS Mean Change from Baseline (SE) [2]	1.27 (1.69)	1.73 (3.04)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.46 (3.56)	
				95% CI for LS Mean Difference [2]	-8.14, 7.22	
				p-value MMRM [2]	0.8995	
				Mean (SD)	2.42 (5.177)	2.46 (4.146)
				Median (MAD)	0.51 (1.410)	4.77 (0.160)
				Mean Difference (SE) [3]	-0.03 (3.325)	
				95% CI for Mean Difference [3]	-7.99, 7.92	
				p-value (Welch's t-test) [3]	0.9915	
				Median Difference (ASE) [4]	2.12 (4.600)	
				95% CI for Median Difference [4]	-10.29, 4.93	
				p-value (Mann-Whitney U test)	0.5791	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.01	
				95% CI for SMD (Hedges' g)	-1.31, 1.30	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Subjects excluded due to known data entry errors.

Table Generation: 11SEP2023 1:01:01 PM

Program: t-qs-cont-peg9-sub.sas

Summary of Z-scores from 9-Hole Pegboard Test by region (excluding subjects with data entry errors)

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	Non-US	Week 24	Absolute value	n (%)	9 (69.23)	4 (80.00)
				Number of patients with missing data: n (%)	4 (30.77)	1 (20.00)
				Mean (SD)	4.00 (3.673)	9.90 (8.199)
				Median (MAD)	3.37 (2.640)	8.42 (4.975)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
NOTE: Subjects excluded due to known data entry errors.
Table Generation: 11SEP2023 1:01:01 PM
Program: t-qs-cont-peg9-sub.sas

Summary of Z-scores from 9-Hole Pegboard Test by region (excluding subjects with data entry errors)

Hand Dominance	Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	Non-US	Week 24	Change from Baseline	n (%)	9 (69.23)	4 (80.00)
				Number of patients with missing data: n (%)	4 (30.77)	1 (20.00)
				LS Mean Change from Baseline (SE) [2]	1.16 (1.08)	1.54 (1.89)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.38 (2.29)	
				95% CI for LS Mean Difference [2]	-5.87, 5.10	
				p-value MMRM [2]	0.8715	
				Mean (SD)	0.91 (2.548)	0.56 (2.842)
				Median (MAD)	0.07 (1.640)	1.89 (0.170)
				Mean Difference (SE) [3]	0.36 (1.581)	
				95% CI for Mean Difference [3]	-3.83, 4.55	
				p-value (Welch's t-test) [3]	0.8379	
				Median Difference (ASE) [4]	0.17 (1.676)	
				95% CI for Median Difference [4]	-3.77, 2.80	
				p-value (Mann-Whitney U test)	0.8170	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.14	
				95% CI for SMD (Hedges' g)	-1.04, 1.31	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Subjects excluded due to known data entry errors.

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4.10.13.8 Summary of Z-scores from 9-Hole Pegboard Test by GMFCS (excluding subjects with data entry errors)

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.5994	
	I	Baseline	Absolute value	n (%)	7 (77.78)	3 (60.00)
				Number of patients with missing data: n (%)	2 (22.22)	2 (40.00)
				Mean (SD)	0.79 (1.671)	2.13 (1.775)
				Median (MAD)	0.93 (1.250)	1.42 (0.600)
		Week 12	Absolute value	n (%)	6 (66.67)	3 (60.00)
				Number of patients with missing data: n (%)	3 (33.33)	2 (40.00)
				Mean (SD)	1.77 (1.433)	2.32 (1.878)
				Median (MAD)	1.10 (0.385)	1.81 (1.060)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Subjects excluded due to known data entry errors.

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Program: t-qs-cont-peg9-sub.sas

Summary of Z-scores from 9-Hole Pegboard Test by GMFCS (excluding subjects with data entry errors)

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	I	Week 12	Change from Baseline	n (%)	6 (66.67)	3 (60.00)
				Number of patients with missing data: n (%)	3 (33.33)	2 (40.00)
				LS Mean Change from Baseline (SE) [2]	0.40 (0.51)	0.40 (0.73)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.00 (0.91)	
				95% CI for LS Mean Difference [2]	-2.16, 2.17	
				p-value MMRM [2]	0.9998	
				Mean (SD)	0.51 (1.415)	0.19 (0.236)
				Median (MAD)	1.05 (0.650)	0.25 (0.140)
				Mean Difference (SE) [3]	0.31 (0.850)	
				95% CI for Mean Difference [3]	-1.17, 1.80	
				p-value (Welch's t-test) [3]	0.6163	
				Median Difference (ASE) [4]	-0.80 (1.041)	
				95% CI for Median Difference [4]	-1.62, 2.00	
				p-value (Mann-Whitney U test)	0.5186	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.26	
				95% CI for SMD (Hedges' g)	-1.13, 1.65	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Subjects excluded due to known data entry errors.

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Program: t-qs-cont-peg9-sub.sas

Summary of Z-scores from 9-Hole Pegboard Test by GMFCS (excluding subjects with data entry errors)

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	I	Week 24	Absolute value	n (%)	5 (55.56)	3 (60.00)
				Number of patients with missing data: n (%)	4 (44.44)	2 (40.00)
				Mean (SD)	1.42 (1.827)	1.48 (0.689)
				Median (MAD)	0.70 (0.720)	1.56 (0.560)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
NOTE: Subjects excluded due to known data entry errors.
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Program: t-qs-cont-peg9-sub.sas

Summary of Z-scores from 9-Hole Pegboard Test by GMFCS (excluding subjects with data entry errors)

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	I	Week 24	Change from Baseline	n (%)	5 (55.56)	3 (60.00)
				Number of patients with missing data: n (%)	4 (44.44)	2 (40.00)
				LS Mean Change from Baseline (SE) [2]	0.07 (0.69)	-0.44 (0.87)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.52 (1.13)	
				95% CI for LS Mean Difference [2]	-2.26, 3.29	
				p-value MMRM [2]	0.6629	
				Mean (SD)	0.20 (1.076)	-0.65 (2.379)
				Median (MAD)	-0.35 (0.550)	0.70 (0.040)
				Mean Difference (SE) [3]	0.85 (1.191)	
				95% CI for Mean Difference [3]	-4.35, 6.05	
				p-value (Welch's t-test) [3]	0.6062	
				Median Difference (ASE) [4]	-0.32 (1.704)	
				95% CI for Median Difference [4]	-5.04, 1.64	
				p-value (Mann-Whitney U test)	0.7656	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.52	
				95% CI for SMD (Hedges' g)	-0.94, 1.99	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Subjects excluded due to known data entry errors.

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Program: t-qs-cont-peg9-sub.sas

Summary of Z-scores from 9-Hole Pegboard Test by GMFCS (excluding subjects with data entry errors)

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	≥ II	Baseline	Absolute value	n (%)	11 (91.67)	6 (100.00)
				Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
				Mean (SD)	3.11 (2.395)	5.32 (4.183)
				Median (MAD)	3.15 (1.150)	4.09 (2.525)
		Week 12	Absolute value	n (%)	10 (83.33)	6 (100.00)
				Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
				Mean (SD)	3.33 (2.371)	5.71 (4.048)
				Median (MAD)	3.46 (1.410)	5.03 (0.975)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Subjects excluded due to known data entry errors.

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Summary of Z-scores from 9-Hole Pegboard Test by GMFCS (excluding subjects with data entry errors)

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	≥ II	Week 12	Change from Baseline	n (%)	10 (83.33)	6 (100.00)
				Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	-0.18 (0.83)	1.02 (1.09)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.21 (1.42)	
				95% CI for LS Mean Difference [2]	-4.25, 1.84	
				p-value MMRM [2]	0.4088	
				Mean (SD)	0.34 (2.947)	0.39 (2.768)
				Median (MAD)	-0.39 (0.910)	1.02 (1.675)
				Mean Difference (SE) [3]	0.05 (1.489)	
				95% CI for Mean Difference [3]	-3.16, 3.27	
				p-value (Welch's t-test) [3]	0.9707	
				Median Difference (ASE) [4]	0.66 (1.870)	
				95% CI for Median Difference [4]	-3.71, 3.46	
				p-value (Mann-Whitney U test)	0.7863	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.02	
				95% CI for SMD (Hedges' g)	-1.03, 0.99	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

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Summary of Z-scores from 9-Hole Pegboard Test by GMFCS (excluding subjects with data entry errors)

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	≥ II	Week 24	Absolute value	n (%)	10 (83.33)	6 (100.00)
				Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
				Mean (SD)	4.77 (3.567)	6.53 (3.682)
				Median (MAD)	3.97 (2.075)	6.49 (2.325)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
NOTE: Subjects excluded due to known data entry errors.
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Summary of Z-scores from 9-Hole Pegboard Test by GMFCS (excluding subjects with data entry errors)

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Dominant Hand	≥ II	Week 24	Change from Baseline	n (%)	10 (83.33)	6 (100.00)
				Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	1.39 (1.08)	1.85 (1.43)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.46 (1.82)	
				95% CI for LS Mean Difference [2]	-4.36, 3.44	
				p-value MMRM [2]	0.8037	
				Mean (SD)	1.43 (4.512)	1.21 (1.456)
				Median (MAD)	0.20 (1.430)	1.15 (0.810)
				Mean Difference (SE) [3]	-0.22 (1.922)	
				95% CI for Mean Difference [3]	-3.60, 3.16	
				p-value (Welch's t-test) [3]	0.8896	
				Median Difference (ASE) [4]	0.94 (1.663)	
				95% CI for Median Difference [4]	-2.97, 3.09	
				p-value (Mann-Whitney U test)	0.5508	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.06	
				95% CI for SMD (Hedges' g)	-0.95, 1.07	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

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[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

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Summary of Z-scores from 9-Hole Pegboard Test by GMFCS (excluding subjects with data entry errors)

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.9095	
	I	Baseline	Absolute value	n (%)	7 (77.78)	3 (60.00)
				Number of patients with missing data: n (%)	2 (22.22)	2 (40.00)
				Mean (SD)	3.25 (5.117)	3.44 (2.167)
				Median (MAD)	2.85 (3.200)	2.53 (0.660)
		Week 12	Absolute value	n (%)	6 (66.67)	3 (60.00)
				Number of patients with missing data: n (%)	3 (33.33)	2 (40.00)
				Mean (SD)	6.79 (11.800)	1.72 (2.011)
				Median (MAD)	2.88 (1.930)	0.96 (0.760)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Summary of Z-scores from 9-Hole Pegboard Test by GMFCS (excluding subjects with data entry errors)

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	I	Week 12	Change from Baseline	n (%)	6 (66.67)	3 (60.00)
				Number of patients with missing data: n (%)	3 (33.33)	2 (40.00)
				LS Mean Change from Baseline (SE) [2]	2.89 (2.32)	-1.69 (3.28)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	4.59 (4.02)	
				95% CI for LS Mean Difference [2]	-5.76, 14.94	
				p-value MMRM [2]	0.3060	
				Mean (SD)	2.90 (7.001)	-1.72 (0.729)
				Median (MAD)	0.76 (0.960)	-1.91 (0.420)
				Mean Difference (SE) [3]	4.62 (4.193)	
				95% CI for Mean Difference [3]	-2.72, 11.96	
				p-value (Welch's t-test) [3]	0.1683	
				Median Difference (ASE) [4]	-2.41 (5.365)	
				95% CI for Median Difference [4]	-18.71, 0.90	
				p-value (Mann-Whitney U test)	0.1556	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.78	
				95% CI for SMD (Hedges' g)	-0.67, 2.22	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

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[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

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Program: t-qs-cont-peg9-sub.sas

Summary of Z-scores from 9-Hole Pegboard Test by GMFCS (excluding subjects with data entry errors)

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	I	Week 24	Absolute value	n (%)	5 (55.56)	3 (60.00)
				Number of patients with missing data: n (%)	4 (44.44)	2 (40.00)
				Mean (SD)	4.32 (6.418)	3.14 (2.076)
				Median (MAD)	2.44 (1.960)	4.17 (0.330)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
NOTE: Subjects excluded due to known data entry errors.
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Summary of Z-scores from 9-Hole Pegboard Test by GMFCS (excluding subjects with data entry errors)

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	I	Week 24	Change from Baseline	n (%)	5 (55.56)	3 (60.00)
				Number of patients with missing data: n (%)	4 (44.44)	2 (40.00)
				LS Mean Change from Baseline (SE) [2]	0.30 (0.80)	-0.27 (0.96)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.58 (1.25)	
				95% CI for LS Mean Difference [2]	-2.74, 3.89	
				p-value MMRM [2]	0.6669	
				Mean (SD)	0.37 (1.200)	-0.30 (1.987)
				Median (MAD)	-0.20 (0.630)	-1.12 (0.620)
				Mean Difference (SE) [3]	0.66 (1.102)	
				95% CI for Mean Difference [3]	-3.45, 4.77	
				p-value (Welch's t-test) [3]	0.6372	
				Median Difference (ASE) [4]	-0.91 (1.648)	
				95% CI for Median Difference [4]	-3.66, 2.80	
				p-value (Mann-Whitney U test)	0.5510	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.44	
				95% CI for SMD (Hedges' g)	-1.01, 1.89	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

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NOTE: Subjects excluded due to known data entry errors.

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Summary of Z-scores from 9-Hole Pegboard Test by GMFCS (excluding subjects with data entry errors)

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	≥ II	Baseline	Absolute value	n (%)	11 (91.67)	6 (100.00)
				Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
				Mean (SD)	2.97 (2.372)	8.42 (7.205)
				Median (MAD)	3.30 (2.130)	5.57 (3.185)
		Week 12	Absolute value	n (%)	9 (75.00)	5 (83.33)
				Number of patients with missing data: n (%)	3 (25.00)	1 (16.67)
				Mean (SD)	5.36 (5.053)	8.97 (8.190)
				Median (MAD)	3.57 (2.730)	5.00 (0.510)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Subjects excluded due to known data entry errors.

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Program: t-qs-cont-peg9-sub.sas

Summary of Z-scores from 9-Hole Pegboard Test by GMFCS (excluding subjects with data entry errors)

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	≥ II	Week 12	Change from Baseline	n (%)	9 (75.00)	5 (83.33)
				Number of patients with missing data: n (%)	3 (25.00)	1 (16.67)
				LS Mean Change from Baseline (SE) [2]	1.42 (1.60)	2.20 (2.24)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.79 (2.88)	
				95% CI for LS Mean Difference [2]	-6.96, 5.38	
				p-value MMRM [2]	0.7887	
				Mean (SD)	2.81 (5.256)	2.07 (2.702)
				Median (MAD)	1.47 (2.620)	1.65 (2.590)
				Mean Difference (SE) [3]	-0.74 (2.547)	
				95% CI for Mean Difference [3]	-5.38, 3.90	
				p-value (Welch's t-test) [3]	0.7336	
				Median Difference (ASE) [4]	0.18 (2.449)	
				95% CI for Median Difference [4]	-5.03, 4.26	
				p-value (Mann-Whitney U test)	1.0000	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.16	
				95% CI for SMD (Hedges' g)	-0.93, 1.26	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Subjects excluded due to known data entry errors.

Table Generation: 11SEP2023 1:01:09 PM

Program: t-qs-cont-peg9-sub.sas

Summary of Z-scores from 9-Hole Pegboard Test by GMFCS (excluding subjects with data entry errors)

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	≥ II	Week 24	Absolute value	n (%)	10 (83.33)	6 (100.00)
				Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
				Mean (SD)	5.28 (3.540)	9.07 (6.680)
				Median (MAD)	5.20 (2.860)	7.98 (4.485)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[3] Based on Welch's t-test
[4] Based on Hodges-Lehmann estimation of the location shift between the two groups
NOTE: Subjects excluded due to known data entry errors.
Table Generation: 11SEP2023 1:01:09 PM
Program: t-qs-cont-peg9-sub.sas

Summary of Z-scores from 9-Hole Pegboard Test by GMFCS (excluding subjects with data entry errors)

Hand Dominance	GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Z-Score - Non-Dominant	≥ II	Week 24	Change from Baseline	n (%)	10 (83.33)	6 (100.00)
				Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
				LS Mean Change from Baseline (SE) [2]	2.44 (1.25)	1.62 (1.80)
				LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.82 (2.33)	
				95% CI for LS Mean Difference [2]	-4.50, 6.14	
				p-value MMRM [2]	0.7337	
				Mean (SD)	2.07 (3.470)	0.65 (2.865)
				Median (MAD)	1.97 (1.945)	1.87 (1.090)
				Mean Difference (SE) [3]	-1.42 (1.687)	
				95% CI for Mean Difference [3]	-4.90, 2.07	
				p-value (Welch's t-test) [3]	0.3944	
				Median Difference (ASE) [4]	-0.80 (2.038)	
				95% CI for Median Difference [4]	-5.41, 2.08	
				p-value (Mann-Whitney U test)	0.4808	
				SMD (Hedges' g) (Pegzilarginase – Placebo)	0.43	
				95% CI for SMD (Hedges' g)	-0.59, 1.46	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; MAD = Median Absolute Deviation; SE = Standard error; ASE = Asymptotic Standard Error; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[3] Based on Welch's t-test

[4] Based on Hodges-Lehmann estimation of the location shift between the two groups

NOTE: Subjects excluded due to known data entry errors.

Table Generation: 11SEP2023 1:01:09 PM

Program: t-qs-cont-peg9-sub.sas

4.10.14Subgruppenanalysen für den Endpunkt WIS

4.10.14.1 Combined Full-Scale IQ Score for subjects who received either WAIS-IV, WISC-V, WPPSI-IV by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.6817	
Male	Baseline	Absolute value	n (%)	9 (42.86)	3 (27.27)
			Number of patients with missing data: n (%)	3 (25.00)	4 (57.14)
			Mean (SD)	62.44 (18.022)	71.33 (27.502)
	Week 24	Absolute value	n (%)	7 (33.33)	5 (45.45)
			Number of patients with missing data: n (%)	5 (41.67)	2 (28.57)
			Mean (SD)	68.71 (20.048)	71.80 (22.376)
		Change from Baseline	n (%)	6 (28.57)	2 (18.18)
			Number of patients with missing data: n (%)	6 (50.00)	5 (71.43)
			LS Mean Change from Baseline (SE) [1]	3.57 (2.551)	4.79 (4.598)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[1]	-1.22 (5.410)	
			95% CI for LS Mean Difference [1]	-15.12, 12.69	
			p-value MMRM [1]	0.8307	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.15	
			95% CI for SMD (Hedges' g)	-1.75, 1.45	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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Table Generation: 11SEP2023 9:07:13 AM

Combined Full-Scale IQ Score for subjects who received either WAIS-IV, WISC-V, WPPSI-IV by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Baseline	Absolute value	n (%)	6 (28.57)	3 (27.27)
			Number of patients with missing data: n (%)	3 (33.33)	1 (25.00)
			Mean (SD)	62.00 (8.718)	48.33 (7.024)
	Week 24	Absolute value	n (%)	7 (33.33)	1 (9.09)
			Number of patients with missing data: n (%)	2 (22.22)	3 (75.00)
			Mean (SD)	67.86 (12.089)	56.00 (-)
		Change from Baseline	n (%)	5 (23.81)	1 (9.09)
			Number of patients with missing data: n (%)	4 (44.44)	3 (75.00)
			LS Mean Change from Baseline (SE) [1]	2.32 (1.847)	12.40 (4.660)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[1]	-10.08 (5.239)	
			95% CI for LS Mean Difference [1]	-26.75, 6.60	
			p-value MMRM [1]	0.1501	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-1.50	
			95% CI for SMD (Hedges' g)	-3.89, 0.88	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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Table Generation: 11SEP2023 9:07:13 AM

4.10.14.2 Combined Full-Scale IQ Score for subjects who received either WAIS-IV, WISC-V, WPPSI-IV by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.7152	
<10.5 years old at screening	Baseline	Absolute value	n (%)	6 (28.57)	2 (18.18)
			Number of patients with missing data: n (%)	6 (50.00)	2 (50.00)
			Mean (SD)	65.83 (15.316)	57.50 (19.092)
	Week 24	Absolute value	n (%)	7 (33.33)	2 (18.18)
			Number of patients with missing data: n (%)	5 (41.67)	2 (50.00)
			Mean (SD)	70.29 (14.941)	71.00 (2.828)
		Change from Baseline	n (%)	4 (19.05)	1 (9.09)
			Number of patients with missing data: n (%)	8 (66.67)	3 (75.00)
			LS Mean Change from Baseline (SE) [1]	3.04 (4.114)	0.84 (8.293)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[1]	2.20 (9.296)	
			95% CI for LS Mean Difference [1]	-37.80, 42.19	
			p-value MMRM [1]	0.8351	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.12	
			95% CI for SMD (Hedges' g)	-2.07, 2.32	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

NOTE: Median age used as cut-off point.

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Table Generation: 11SEP2023 9:07:44 AM

Combined Full-Scale IQ Score for subjects who received either WAIS-IV, WISC-V, WPPSI-IV by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	9 (42.86)	4 (36.36)
			Number of patients with missing data: n (%)	0 (0.00)	3 (42.86)
			Mean (SD)	59.89 (14.487)	61.00 (25.974)
	Week 24	Absolute value	n (%)	7 (33.33)	4 (36.36)
			Number of patients with missing data: n (%)	2 (22.22)	3 (42.86)
			Mean (SD)	66.29 (17.774)	68.25 (27.035)
		Change from Baseline	n (%)	7 (33.33)	2 (18.18)
			Number of patients with missing data: n (%)	2 (22.22)	5 (71.43)
			LS Mean Change from Baseline (SE) [1]	4.28 (1.601)	6.01 (3.061)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[1]	-1.73 (3.501)	
			95% CI for LS Mean Difference [1]	-10.29, 6.84	
			p-value MMRM [1]	0.6389	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.33	
			95% CI for SMD (Hedges' g)	-1.91, 1.25	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
Program: t-fullscaleIQ-sub.sas
Table Generation: 11SEP2023 9:07:44 AM

4.10.14.3 Combined Full-Scale IQ Score for subjects who received either WAIS-IV, WISC-V, WPPSI-IV by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.4929	
US	Baseline	Absolute value	n (%)	6 (28.57)	4 (36.36)
			Number of patients with missing data: n (%)	2 (25.00)	2 (33.33)
			Mean (SD)	65.83 (14.470)	63.75 (27.097)
	Week 24	Absolute value	n (%)	6 (28.57)	3 (27.27)
			Number of patients with missing data: n (%)	2 (25.00)	3 (50.00)
			Mean (SD)	74.00 (8.485)	82.33 (19.732)
		Change from Baseline	n (%)	5 (23.81)	2 (18.18)
			Number of patients with missing data: n (%)	3 (37.50)	4 (66.67)
			LS Mean Change from Baseline (SE) [1]	4.46 (3.077)	6.36 (5.166)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[1]	-1.90 (6.338)	
			95% CI for LS Mean Difference [1]	-19.50, 15.70	
			p-value MMRM [1]	0.7794	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.19	
			95% CI for SMD (Hedges' g)	-1.84, 1.45	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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Table Generation: 11SEP2023 9:08:14 AM

Combined Full-Scale IQ Score for subjects who received either WAIS-IV, WISC-V, WPPSI-IV by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Baseline	Absolute value	n (%)	9 (42.86)	2 (18.18)
			Number of patients with missing data: n (%)	4 (30.77)	3 (60.00)
			Mean (SD)	59.89 (15.020)	52.00 (4.243)
	Week 24	Absolute value	n (%)	8 (38.10)	3 (27.27)
			Number of patients with missing data: n (%)	5 (38.46)	2 (40.00)
			Mean (SD)	64.00 (19.228)	56.00 (14.000)
		Change from Baseline	n (%)	6 (28.57)	1 (9.09)
			Number of patients with missing data: n (%)	7 (53.85)	4 (80.00)
			LS Mean Change from Baseline (SE) [1]	1.81 (1.277)	9.14 (3.286)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[1]	-7.33 (3.582)	
			95% CI for LS Mean Difference [1]	-17.28, 2.61	
			p-value MMRM [1]	0.1100	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-1.65	
			95% CI for SMD (Hedges' g)	-4.01, 0.70	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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Table Generation: 11SEP2023 9:08:14 AM

4.10.14.4 Combined Full-Scale IQ Score for subjects who received either WAIS-IV, WISC-V, WPPSI-IV by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	Not applicable	
I	Baseline	Absolute value	n (%)	8 (38.10)	5 (45.45)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	67.50 (15.884)	63.00 (22.935)
	Week 24	Absolute value	n (%)	6 (28.57)	3 (27.27)
			Number of patients with missing data: n (%)	3 (33.33)	2 (40.00)
			Mean (SD)	74.33 (15.591)	78.00 (24.880)
		Change from Baseline	n (%)	6 (28.57)	3 (27.27)
			Number of patients with missing data: n (%)	3 (33.33)	2 (40.00)
			LS Mean Change from Baseline (SE) [1]	2.15 (2.426)	5.03 (3.431)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[1]	-2.87 (4.202)	
			95% CI for LS Mean Difference [1]	-13.15, 7.41	
			p-value MMRM [1]	0.5200	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.39	
			95% CI for SMD (Hedges' g)	-1.79, 1.01	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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Table Generation: 11SEP2023 9:08:46 AM

Combined Full-Scale IQ Score for subjects who received either WAIS-IV, WISC-V, WPPSI-IV by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Baseline	Absolute value	n (%)	7 (33.33)	1 (9.09)
			Number of patients with missing data: n (%)	5 (41.67)	5 (83.33)
			Mean (SD)	56.29 (11.131)	44.00 (-)
	Week 24	Absolute value	n (%)	8 (38.10)	3 (27.27)
			Number of patients with missing data: n (%)	4 (33.33)	3 (50.00)
			Mean (SD)	63.75 (15.545)	60.33 (15.885)
		Change from Baseline	n (%)	5 (23.81)	0 (0.00)
			Number of patients with missing data: n (%)	7 (58.33)	6 (100.00)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

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Table Generation: 11SEP2023 9:08:46 AM

4.10.14.5 Combined Full-Scale IQ Score for subjects who received either WAIS-IV, WISC-V, WPPSI-IV by gender (excluding subjects with inconsistent or not verifiable data)

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.9240	
Male	Baseline	Absolute value	n (%)	8 (38.10)	2 (18.18)
			Number of patients with missing data: n (%)	4 (33.33)	5 (71.43)
			Mean (SD)	63.00 (19.183)	71.50 (38.891)
	Week 24	Absolute value	n (%)	6 (28.57)	4 (36.36)
			Number of patients with missing data: n (%)	6 (50.00)	3 (42.86)
			Mean (SD)	69.33 (21.888)	71.50 (25.826)
		Change from Baseline	n (%)	5 (23.81)	1 (9.09)
			Number of patients with missing data: n (%)	7 (58.33)	6 (85.71)
			LS Mean Change from Baseline (SE) [1]	2.74 (3.389)	8.30 (8.487)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[1]	-5.55 (9.530)	
			95% CI for LS Mean Difference [1]	-35.88, 24.77	
			p-value MMRM [1]	0.6009	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.45	
			95% CI for SMD (Hedges' g)	-2.62, 1.72	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
Program: t-fullscaleIQ-sub.sas
Table Generation: 11SEP2023 9:09:21 AM

Combined Full-Scale IQ Score for subjects who received either WAIS-IV, WISC-V, WPPSI-IV by gender (excluding subjects with inconsistent or not verifiable data)

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Baseline	Absolute value	n (%)	6 (28.57)	3 (27.27)
			Number of patients with missing data: n (%)	3 (33.33)	1 (25.00)
			Mean (SD)	62.00 (8.718)	48.33 (7.024)
	Week 24	Absolute value	n (%)	6 (28.57)	1 (9.09)
			Number of patients with missing data: n (%)	3 (33.33)	3 (75.00)
			Mean (SD)	67.33 (13.155)	56.00 (-)
		Change from Baseline	n (%)	5 (23.81)	1 (9.09)
			Number of patients with missing data: n (%)	4 (44.44)	3 (75.00)
			LS Mean Change from Baseline (SE) [1]	2.32 (1.847)	12.40 (4.660)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[1]	-10.08 (5.239)	
			95% CI for LS Mean Difference [1]	-26.75, 6.60	
			p-value MMRM [1]	0.1501	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-1.50	
			95% CI for SMD (Hedges' g)	-3.89, 0.88	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
Program: t-fullscaleIQ-sub.sas
Table Generation: 11SEP2023 9:09:21 AM

4.10.14.6 Combined Full-Scale IQ Score for subjects who received either WAIS-IV, WISC-V, WPPSI-IV by age group (excluding subjects with inconsistent or not verifiable data)

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	Not applicable	
<10.5 years old at screening	Baseline	Absolute value	n (%)	6 (28.57)	1 (9.09)
			Number of patients with missing data: n (%)	6 (50.00)	3 (75.00)
			Mean (SD)	65.83 (15.316)	44.00 (-)
	Week 24	Absolute value	n (%)	6 (28.57)	1 (9.09)
			Number of patients with missing data: n (%)	6 (50.00)	3 (75.00)
			Mean (SD)	70.17 (16.364)	69.00 (-)
		Change from Baseline	n (%)	4 (19.05)	0 (0.00)
			Number of patients with missing data: n (%)	8 (66.67)	4 (100.00)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
Program: t-fullscaleIQ-sub.sas
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Combined Full-Scale IQ Score for subjects who received either WAIS-IV, WISC-V, WPPSI-IV by age group (excluding subjects with inconsistent or not verifiable data)

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Baseline	Absolute value	n (%)	8 (38.10)	4 (36.36)
			Number of patients with missing data: n (%)	1 (11.11)	3 (42.86)
			Mean (SD)	60.13 (15.468)	61.00 (25.974)
	Week 24	Absolute value	n (%)	6 (28.57)	4 (36.36)
			Number of patients with missing data: n (%)	3 (33.33)	3 (42.86)
			Mean (SD)	66.50 (19.460)	68.25 (27.035)
		Change from Baseline	n (%)	6 (28.57)	2 (18.18)
			Number of patients with missing data: n (%)	3 (33.33)	5 (71.43)
			LS Mean Change from Baseline (SE) [1]	3.83 (1.792)	6.01 (3.156)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[1]	-2.18 (3.675)	
			95% CI for LS Mean Difference [1]	-11.63, 7.27	
			p-value MMRM [1]	0.5789	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.38	
			95% CI for SMD (Hedges' g)	-1.99, 1.24	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
Program: t-fullscaleIQ-sub.sas
Table Generation: 11SEP2023 9:09:48 AM

4.10.14.7 Combined Full-Scale IQ Score for subjects who received either WAIS-IV, WISC-V, WPPSI-IV by region (excluding subjects with inconsistent or not verifiable data)

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.8064	
US	Baseline	Absolute value	n (%)	5 (23.81)	3 (27.27)
			Number of patients with missing data: n (%)	3 (37.50)	3 (50.00)
			Mean (SD)	67.40 (15.598)	61.33 (32.655)
	Week 24	Absolute value	n (%)	4 (19.05)	2 (18.18)
			Number of patients with missing data: n (%)	4 (50.00)	4 (66.67)
			Mean (SD)	77.00 (8.832)	87.00 (25.456)
		Change from Baseline	n (%)	4 (19.05)	1 (9.09)
			Number of patients with missing data: n (%)	4 (50.00)	5 (83.33)
			LS Mean Change from Baseline (SE) [1]	2.42 (3.573)	16.33 (8.823)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[1]	-13.91 (10.415)	
			95% CI for LS Mean Difference [1]	-58.72, 30.90	
			p-value MMRM [1]	0.3134	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.89	
			95% CI for SMD (Hedges' g)	-3.19, 1.42	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
Program: t-fullscaleIQ-sub.sas
Table Generation: 11SEP2023 9:10:17 AM

Combined Full-Scale IQ Score for subjects who received either WAIS-IV, WISC-V, WPPSI-IV by region (excluding subjects with inconsistent or not verifiable data)

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Baseline	Absolute value	n (%)	9 (42.86)	2 (18.18)
			Number of patients with missing data: n (%)	4 (30.77)	3 (60.00)
			Mean (SD)	59.89 (15.020)	52.00 (4.243)
	Week 24	Absolute value	n (%)	8 (38.10)	3 (27.27)
			Number of patients with missing data: n (%)	5 (38.46)	2 (40.00)
			Mean (SD)	64.00 (19.228)	56.00 (14.000)
		Change from Baseline	n (%)	6 (28.57)	1 (9.09)
			Number of patients with missing data: n (%)	7 (53.85)	4 (80.00)
			LS Mean Change from Baseline (SE) [1]	1.81 (1.277)	9.14 (3.286)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[1]	-7.33 (3.582)	
			95% CI for LS Mean Difference [1]	-17.28, 2.61	
			p-value MMRM [1]	0.1100	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-1.65	
			95% CI for SMD (Hedges' g)	-4.01, 0.70	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
Program: t-fullscaleIQ-sub.sas
Table Generation: 11SEP2023 9:10:17 AM

4.10.14.8 Combined Full-Scale IQ Score for subjects who received either WAIS-IV, WISC-V, WPPSI-IV by GMFCS (excluding subjects with inconsistent or not verifiable data)

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	Not applicable	
I	Baseline	Absolute value	n (%)	8 (38.10)	4 (36.36)
			Number of patients with missing data: n (%)	1 (11.11)	1 (20.00)
			Mean (SD)	67.50 (15.884)	61.00 (25.974)
	Week 24	Absolute value	n (%)	6 (28.57)	2 (18.18)
			Number of patients with missing data: n (%)	3 (33.33)	3 (60.00)
			Mean (SD)	74.33 (15.591)	80.50 (34.648)
		Change from Baseline	n (%)	6 (28.57)	2 (18.18)
			Number of patients with missing data: n (%)	3 (33.33)	3 (60.00)
			LS Mean Change from Baseline (SE) [1]	2.14 (2.566)	6.57 (4.447)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[1]	-4.42 (5.136)	
			95% CI for LS Mean Difference [1]	-17.63, 8.78	
			p-value MMRM [1]	0.4285	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.54	
			95% CI for SMD (Hedges' g)	-2.17, 1.09	

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
Program: t-fullscaleIQ-sub.sas
Table Generation: 11SEP2023 9:10:43 AM

Combined Full-Scale IQ Score for subjects who received either WAIS-IV, WISC-V, WPPSI-IV by GMFCS (excluding subjects with inconsistent or not verifiable data)

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Baseline	Absolute value	n (%)	6 (28.57)	1 (9.09)
			Number of patients with missing data: n (%)	6 (50.00)	5 (83.33)
			Mean (SD)	56.00 (12.166)	44.00 (-)
	Week 24	Absolute value	n (%)	6 (28.57)	3 (27.27)
			Number of patients with missing data: n (%)	6 (50.00)	3 (50.00)
			Mean (SD)	62.33 (18.030)	60.33 (15.885)
		Change from Baseline	n (%)	4 (19.05)	0 (0.00)
			Number of patients with missing data: n (%)	8 (66.67)	6 (100.00)

Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.

[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.

Program: t-fullscaleIQ-sub.sas

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4.10.15 Subgruppenanalysen für den Peds-QL

4.10.15.1 Pediatric Quality of Life Inventory (PEDSQL) - Physical Functioning by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.2098	
Male	Baseline	Self-report	n (%)	7 (58.33)	2 (40.00)
		Parent Report	n (%)	4 (33.33)	3 (60.00)
		Absolute value	n (%)	11 (91.67)	5 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	73.01 (25.048)	51.88 (21.148)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Physical Functioning Scale Score values for patient 129-0001 were calculated after data-base lock.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Functioning by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Male	Week 12	Self-report	n (%)	7 (58.33)	1 (20.00)
		Parent Report	n (%)	4 (33.33)	3 (60.00)
		Absolute value	n (%)	11 (91.67)	4 (80.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (20.00)
			Mean (SD)	65.34 (24.506)	44.53 (13.592)
		Change from Baseline	n (%)	11 (91.67)	4 (80.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	-5.86 (5.749)	-24.95 (9.547)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	19.09 (11.235)	
			95% CI for LS Mean Difference [2]	-5.79, 43.97	
			p-value MMRM [2]	0.1188	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.88	
			95% CI for SMD (Hedges' g)	-0.31, 2.08	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Physical Functioning Scale Score values for patient 129-0001 were calculated after data-base lock.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Functioning by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Male	Week 24	Self-report	n (%)	6 (50.00)	1 (20.00)
		Parent Report	n (%)	3 (25.00)	4 (80.00)
		Absolute value	n (%)	9 (75.00)	5 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			Mean (SD)	75.00 (21.819)	49.38 (10.680)
		Change from Baseline	n (%)	9 (75.00)	5 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	1.04 (6.808)	-16.73 (9.430)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	17.77 (12.016)	
			95% CI for LS Mean Difference [2]	-8.96, 44.50	
			p-value MMRM [2]	0.1696	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.76	
			95% CI for SMD (Hedges' g)	-0.38, 1.89	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Physical Functioning Scale Score values for patient 129-0001 were calculated after data-base lock.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Functioning by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Baseline	Self-report	n (%)	3 (37.50)	3 (75.00)
		Parent Report	n (%)	5 (62.50)	1 (25.00)
		Absolute value	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	69.53 (22.654)	84.39 (23.112)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Physical Functioning Scale Score values for patient 129-0001 were calculated after data-base lock.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Functioning by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Week 12	Self-report	n (%)	3 (37.50)	3 (75.00)
		Parent Report	n (%)	5 (62.50)	0 (0.00)
		Absolute value	n (%)	8 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			Mean (SD)	62.49 (24.191)	80.21 (13.002)
		Change from Baseline	n (%)	8 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	-8.95 (7.845)	4.05 (12.974)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-13.00 (15.327)	
			95% CI for LS Mean Difference [2]	-48.07, 22.06	
			p-value MMRM [2]	0.4198	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.50	
			95% CI for SMD (Hedges' g)	-1.85, 0.85	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Physical Functioning Scale Score values for patient 129-0001 were calculated after data-base lock.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Functioning by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Week 24	Self-report	n (%)	3 (37.50)	3 (75.00)
		Parent Report	n (%)	5 (62.50)	0 (0.00)
		Absolute value	n (%)	8 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			Mean (SD)	67.71 (21.465)	65.62 (21.875)
		Change from Baseline	n (%)	8 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	-3.73 (7.125)	-10.54 (11.814)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	6.81 (13.977)	
			95% CI for LS Mean Difference [2]	-25.36, 38.98	
			p-value MMRM [2]	0.6391	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.29	
			95% CI for SMD (Hedges' g)	-1.05, 1.62	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Physical Functioning Scale Score values for patient 129-0001 were calculated after data-base lock.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.15.2 Pediatric Quality of Life Inventory (PEDSQL) - Physical Functioning by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.3423	
<10.5 years old at screening	Baseline	Self-report	n (%)	3 (25.00)	1 (25.00)
		Parent Report	n (%)	8 (66.67)	3 (75.00)
		Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	74.71 (19.991)	67.97 (20.786)

NOTE: If available, self-report was used and if no self report was available parent report was used. Median age used as cut-off point.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Physical Functioning Scale Score values for patient 129-0001 were calculated after data-base lock.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
Program: t-qs-cont-sub.sas
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Functioning by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
<10.5 years old at screening	Week 12	Self-report	n (%)	3 (25.00)	0 (0.00)
		Parent Report	n (%)	8 (66.67)	3 (75.00)
		Absolute value	n (%)	11 (91.67)	3 (75.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (25.00)
			Mean (SD)	64.77 (26.437)	46.88 (15.625)
		Change from Baseline	n (%)	11 (91.67)	3 (75.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	-7.55 (7.833)	-25.93 (15.012)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	18.38 (16.992)	
			95% CI for LS Mean Difference [2]	-19.20, 55.96	
			p-value MMRM [2]	0.3034	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.63	
			95% CI for SMD (Hedges' g)	-0.67, 1.93	

NOTE: If available, self-report was used and if no self report was available parent report was used. Median age used as cut-off point.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Physical Functioning Scale Score values for patient 129-0001 were calculated after data-base lock.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Functioning by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
<10.5 years old at screening	Week 24	Self-report	n (%)	3 (25.00)	0 (0.00)
		Parent Report	n (%)	6 (50.00)	3 (75.00)
		Absolute value	n (%)	9 (75.00)	3 (75.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
			Mean (SD)	80.33 (18.075)	56.25 (5.413)
		Change from Baseline	n (%)	9 (75.00)	3 (75.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	6.94 (5.711)	-16.56 (10.260)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	23.50 (11.783)	
			95% CI for LS Mean Difference [2]	-3.17, 50.17	
			p-value MMRM [2]	0.0774	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.19	
			95% CI for SMD (Hedges' g)	-0.22, 2.59	

NOTE: If available, self-report was used and if no self report was available parent report was used. Median age used as cut-off point.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Physical Functioning Scale Score values for patient 129-0001 were calculated after data-base lock.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Functioning by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Baseline	Self-report	n (%)	7 (87.50)	4 (80.00)
		Parent Report	n (%)	1 (12.50)	1 (20.00)
		Absolute value	n (%)	8 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	67.19 (28.446)	65.01 (33.259)

NOTE: If available, self-report was used and if no self report was available parent report was used. Median age used as cut-off point.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Physical Functioning Scale Score values for patient 129-0001 were calculated after data-base lock.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Functioning by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Week 12	Self-report	n (%)	7 (87.50)	4 (80.00)
		Parent Report	n (%)	1 (12.50)	0 (0.00)
		Absolute value	n (%)	8 (100.00)	4 (80.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (20.00)
			Mean (SD)	63.28 (21.179)	69.53 (23.848)
		Change from Baseline	n (%)	8 (100.00)	4 (80.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	-5.74 (5.312)	-3.60 (7.166)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-2.13 (8.908)	
			95% CI for LS Mean Difference [2]	-22.55, 18.28	
			p-value MMRM [2]	0.8164	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.12	
			95% CI for SMD (Hedges' g)	-1.32, 1.08	

NOTE: If available, self-report was used and if no self report was available parent report was used. Median age used as cut-off point.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Physical Functioning Scale Score values for patient 129-0001 were calculated after data-base lock.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Functioning by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Week 24	Self-report	n (%)	6 (75.00)	4 (80.00)
		Parent Report	n (%)	2 (25.00)	1 (20.00)
		Absolute value	n (%)	8 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	61.72 (21.311)	55.00 (21.483)
		Change from Baseline	n (%)	8 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-9.82 (5.694)	-13.14 (7.221)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.33 (9.240)	
			95% CI for LS Mean Difference [2]	-17.31, 23.96	
			p-value MMRM [2]	0.7266	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.18	
			95% CI for SMD (Hedges' g)	-0.94, 1.30	

NOTE: If available, self-report was used and if no self report was available parent report was used. Median age used as cut-off point.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Physical Functioning Scale Score values for patient 129-0001 were calculated after data-base lock.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.15.3 Pediatric Quality of Life Inventory (PEDSQL) - Physical Functioning by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.9446	
US	Baseline	Self-report	n (%)	4 (50.00)	2 (50.00)
		Parent Report	n (%)	4 (50.00)	2 (50.00)
		Absolute value	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	75.79 (22.085)	67.98 (20.807)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Physical Functioning Scale Score values for patient 129-0001 were calculated after data-base lock.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Functioning by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
US	Week 12	Self-report	n (%)	4 (50.00)	1 (25.00)
		Parent Report	n (%)	4 (50.00)	3 (75.00)
		Absolute value	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	67.19 (24.206)	57.81 (25.312)
		Change from Baseline	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-8.35 (7.457)	-16.91 (10.548)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	8.56 (12.921)	
			95% CI for LS Mean Difference [2]	-20.68, 37.81	
			p-value MMRM [2]	0.5241	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.35	
			95% CI for SMD (Hedges' g)	-0.86, 1.56	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Physical Functioning Scale Score values for patient 129-0001 were calculated after data-base lock.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Functioning by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
US	Week 24	Self-report	n (%)	4 (50.00)	1 (25.00)
		Parent Report	n (%)	4 (50.00)	3 (75.00)
		Absolute value	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	75.78 (21.698)	64.06 (16.238)
		Change from Baseline	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.24 (6.570)	-10.66 (9.295)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	10.90 (11.387)	
			95% CI for LS Mean Difference [2]	-14.86, 36.66	
			p-value MMRM [2]	0.3634	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.51	
			95% CI for SMD (Hedges' g)	-0.71, 1.73	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Physical Functioning Scale Score values for patient 129-0001 were calculated after data-base lock.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Functioning by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Baseline	Self-report	n (%)	6 (50.00)	3 (60.00)
		Parent Report	n (%)	5 (41.67)	2 (40.00)
		Absolute value	n (%)	11 (91.67)	5 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	68.46 (25.020)	65.00 (33.249)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Physical Functioning Scale Score values for patient 129-0001 were calculated after data-base lock.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Functioning by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Week 12	Self-report	n (%)	6 (50.00)	3 (60.00)
		Parent Report	n (%)	5 (41.67)	0 (0.00)
		Absolute value	n (%)	11 (91.67)	3 (60.00)
			Number of patients with missing data: n (%)	1 (8.33)	2 (40.00)
			Mean (SD)	61.92 (24.309)	62.51 (23.605)
		Change from Baseline	n (%)	11 (91.67)	3 (60.00)
			Number of patients with missing data: n (%)	1 (8.33)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-6.13 (6.659)	-6.72 (12.599)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.58 (14.256)	
			95% CI for LS Mean Difference [2]	-30.57, 31.73	
			p-value MMRM [2]	0.9680	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.02	
			95% CI for SMD (Hedges' g)	-1.25, 1.30	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Physical Functioning Scale Score values for patient 129-0001 were calculated after data-base lock.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Functioning by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Week 24	Self-report	n (%)	5 (41.67)	3 (60.00)
		Parent Report	n (%)	4 (33.33)	1 (20.00)
		Absolute value	n (%)	9 (75.00)	4 (80.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (20.00)
			Mean (SD)	67.83 (21.492)	46.88 (13.239)
		Change from Baseline	n (%)	9 (75.00)	4 (80.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	-1.86 (6.643)	-18.68 (10.165)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	16.82 (12.288)	
			95% CI for LS Mean Difference [2]	-10.61, 44.24	
			p-value MMRM [2]	0.2015	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.74	
			95% CI for SMD (Hedges' g)	-0.48, 1.96	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Physical Functioning Scale Score values for patient 129-0001 were calculated after data-base lock.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.15.4 Pediatric Quality of Life Inventory (PEDSQL) - Physical Functioning by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.4654	
I	Baseline	Self-report	n (%)	5 (55.56)	4 (100.00)
		Parent Report	n (%)	3 (33.33)	0 (0.00)
		Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	88.68 (11.568)	72.67 (28.122)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Physical Functioning Scale Score values for patient 129-0001 were calculated after data-base lock.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Functioning by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
I	Week 12	Self-report	n (%)	5 (55.56)	3 (75.00)
		Parent Report	n (%)	3 (33.33)	1 (25.00)
		Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	73.44 (20.044)	75.78 (13.824)
		Change from Baseline	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-13.24 (6.438)	-7.12 (9.259)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-6.13 (11.526)	
			95% CI for LS Mean Difference [2]	-32.05, 19.79	
			p-value MMRM [2]	0.6072	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.29	
			95% CI for SMD (Hedges' g)	-1.50, 0.92	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Physical Functioning Scale Score values for patient 129-0001 were calculated after data-base lock.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Functioning by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
I	Week 24	Self-report	n (%)	5 (55.56)	3 (75.00)
		Parent Report	n (%)	3 (33.33)	1 (25.00)
		Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	79.30 (16.697)	64.06 (18.131)
		Change from Baseline	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-7.39 (6.119)	-18.84 (8.816)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	11.45 (10.993)	
			95% CI for LS Mean Difference [2]	-13.37, 36.28	
			p-value MMRM [2]	0.3243	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.57	
			95% CI for SMD (Hedges' g)	-0.66, 1.80	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Physical Functioning Scale Score values for patient 129-0001 were calculated after data-base lock.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Functioning by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Baseline	Self-report	n (%)	5 (45.45)	1 (20.00)
		Parent Report	n (%)	6 (54.55)	4 (80.00)
		Absolute value	n (%)	11 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	59.09 (22.206)	61.25 (27.740)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Physical Functioning Scale Score values for patient 129-0001 were calculated after data-base lock.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Functioning by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Week 12	Self-report	n (%)	5 (45.45)	1 (20.00)
		Parent Report	n (%)	6 (54.55)	2 (40.00)
		Absolute value	n (%)	11 (100.00)	3 (60.00)
			Number of patients with missing data: n (%)	0 (0.00)	2 (40.00)
			Mean (SD)	57.38 (24.763)	38.54 (7.867)
		Change from Baseline	n (%)	11 (100.00)	3 (60.00)
			Number of patients with missing data: n (%)	0 (0.00)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-1.57 (6.499)	-22.45 (12.256)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	20.89 (13.872)	
			95% CI for LS Mean Difference [2]	-9.40, 51.18	
			p-value MMRM [2]	0.1585	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.87	
			95% CI for SMD (Hedges' g)	-0.46, 2.19	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Physical Functioning Scale Score values for patient 129-0001 were calculated after data-base lock.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Functioning by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Week 24	Self-report	n (%)	4 (36.36)	1 (20.00)
		Parent Report	n (%)	5 (45.45)	3 (60.00)
		Absolute value	n (%)	9 (81.82)	4 (80.00)
			Number of patients with missing data: n (%)	2 (18.18)	1 (20.00)
			Mean (SD)	64.70 (23.465)	46.88 (10.508)
		Change from Baseline	n (%)	9 (81.82)	4 (80.00)
			Number of patients with missing data: n (%)	2 (18.18)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	4.84 (7.185)	-10.86 (10.924)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	15.70 (13.155)	
			95% CI for LS Mean Difference [2]	-13.69, 45.09	
			p-value MMRM [2]	0.2607	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.64	
			95% CI for SMD (Hedges' g)	-0.57, 1.85	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Physical Functioning Scale Score values for patient 129-0001 were calculated after data-base lock.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.15.5 Pediatric Quality of Life Inventory (PEDSQL) - Emotional Functioning by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.2724	
Male	Baseline	Self-report	n (%)	7 (58.33)	2 (40.00)
		Parent Report	n (%)	4 (33.33)	3 (60.00)
		Absolute value	n (%)	11 (91.67)	5 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	75.91 (22.674)	63.00 (22.528)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Emotional Functioning by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Male	Week 12	Self-report	n (%)	7 (58.33)	1 (20.00)
		Parent Report	n (%)	4 (33.33)	3 (60.00)
		Absolute value	n (%)	11 (91.67)	4 (80.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (20.00)
			Mean (SD)	75.45 (15.404)	68.75 (20.966)
		Change from Baseline	n (%)	11 (91.67)	4 (80.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	0.79 (3.937)	-0.53 (6.274)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.32 (7.473)	
			95% CI for LS Mean Difference [2]	-14.79, 17.43	
			p-value MMRM [2]	0.8626	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.09	
			95% CI for SMD (Hedges' g)	-1.05, 1.24	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Emotional Functioning by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Male	Week 24	Self-report	n (%)	6 (50.00)	1 (20.00)
		Parent Report	n (%)	3 (25.00)	4 (80.00)
		Absolute value	n (%)	9 (75.00)	5 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			Mean (SD)	79.44 (12.105)	62.00 (23.076)
		Change from Baseline	n (%)	9 (75.00)	5 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	4.69 (4.405)	-7.24 (6.415)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	11.93 (7.829)	
			95% CI for LS Mean Difference [2]	-5.03, 28.88	
			p-value MMRM [2]	0.1521	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.79	
			95% CI for SMD (Hedges' g)	-0.35, 1.93	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Emotional Functioning by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Baseline	Self-report	n (%)	3 (37.50)	3 (75.00)
		Parent Report	n (%)	5 (62.50)	1 (25.00)
		Absolute value	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	53.75 (20.133)	71.25 (20.156)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Emotional Functioning by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Week 12	Self-report	n (%)	3 (37.50)	3 (75.00)
		Parent Report	n (%)	5 (62.50)	0 (0.00)
		Absolute value	n (%)	8 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			Mean (SD)	66.25 (26.288)	58.33 (10.408)
		Change from Baseline	n (%)	8 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	12.73 (6.889)	-20.62 (11.997)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	33.35 (14.569)	
			95% CI for LS Mean Difference [2]	0.30, 66.40	
			p-value MMRM [2]	0.0483 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.44	
			95% CI for SMD (Hedges' g)	-0.04, 2.93	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Emotional Functioning by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Week 24	Self-report	n (%)	3 (37.50)	3 (75.00)
		Parent Report	n (%)	5 (62.50)	0 (0.00)
		Absolute value	n (%)	8 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			Mean (SD)	73.13 (25.903)	71.67 (30.139)
		Change from Baseline	n (%)	8 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	19.61 (6.044)	-7.29 (10.714)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	26.89 (13.122)	
			95% CI for LS Mean Difference [2]	-3.21, 57.00	
			p-value MMRM [2]	0.0735	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.31	
			95% CI for SMD (Hedges' g)	-0.15, 2.77	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.15.6 Pediatric Quality of Life Inventory (PEDSQL) - Emotional Functioning by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.0400 ***	
<10.5 years old at screening	Baseline	Self-report	n (%)	3 (25.00)	1 (25.00)
		Parent Report	n (%)	8 (66.67)	3 (75.00)
		Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	59.09 (20.472)	55.00 (9.129)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Emotional Functioning by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
<10.5 years old at screening	Week 12	Self-report	n (%)	3 (25.00)	0 (0.00)
		Parent Report	n (%)	8 (66.67)	3 (75.00)
		Absolute value	n (%)	11 (91.67)	3 (75.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (25.00)
			Mean (SD)	74.09 (21.309)	58.33 (2.887)
		Change from Baseline	n (%)	11 (91.67)	3 (75.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	15.01 (4.230)	-0.18 (8.101)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	15.19 (9.139)	
			95% CI for LS Mean Difference [2]	-4.85, 35.23	
			p-value MMRM [2]	0.1238	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.97	
			95% CI for SMD (Hedges' g)	-0.37, 2.30	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Emotional Functioning by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
<10.5 years old at screening	Week 24	Self-report	n (%)	3 (25.00)	0 (0.00)
		Parent Report	n (%)	6 (50.00)	3 (75.00)
		Absolute value	n (%)	9 (75.00)	3 (75.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
			Mean (SD)	80.00 (21.651)	48.33 (7.638)
		Change from Baseline	n (%)	9 (75.00)	3 (75.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	20.60 (4.298)	-10.18 (7.681)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	30.78 (8.802)	
			95% CI for LS Mean Difference [2]	11.20, 50.36	
			p-value MMRM [2]	0.0057 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	2.10	
			95% CI for SMD (Hedges' g)	0.50, 3.70	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Emotional Functioning by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Baseline	Self-report	n (%)	7 (87.50)	4 (80.00)
		Parent Report	n (%)	1 (12.50)	1 (20.00)
		Absolute value	n (%)	8 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	76.88 (25.626)	76.00 (23.292)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Emotional Functioning by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Week 12	Self-report	n (%)	7 (87.50)	4 (80.00)
		Parent Report	n (%)	1 (12.50)	0 (0.00)
		Absolute value	n (%)	8 (100.00)	4 (80.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (20.00)
			Mean (SD)	68.13 (20.343)	68.75 (22.500)
		Change from Baseline	n (%)	8 (100.00)	4 (80.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	-8.87 (5.019)	-11.41 (6.981)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.54 (8.601)	
			95% CI for LS Mean Difference [2]	-16.53, 21.61	
			p-value MMRM [2]	0.7739	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.16	
			95% CI for SMD (Hedges' g)	-1.04, 1.36	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Emotional Functioning by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Week 24	Self-report	n (%)	6 (75.00)	4 (80.00)
		Parent Report	n (%)	2 (25.00)	1 (20.00)
		Absolute value	n (%)	8 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	72.50 (17.113)	76.00 (25.348)
		Change from Baseline	n (%)	8 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-3.31 (5.047)	-0.44 (6.370)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-2.87 (8.117)	
			95% CI for LS Mean Difference [2]	-20.86, 15.12	
			p-value MMRM [2]	0.7309	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.18	
			95% CI for SMD (Hedges' g)	-1.30, 0.94	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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4.10.15.7 Pediatric Quality of Life Inventory (PEDSQL) - Emotional Functioning by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.6719	
US	Baseline	Self-report	n (%)	4 (50.00)	2 (50.00)
		Parent Report	n (%)	4 (50.00)	2 (50.00)
		Absolute value	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	68.13 (26.178)	62.50 (14.434)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Emotional Functioning by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
US	Week 12	Self-report	n (%)	4 (50.00)	1 (25.00)
		Parent Report	n (%)	4 (50.00)	3 (75.00)
		Absolute value	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	76.88 (22.668)	61.25 (6.292)
		Change from Baseline	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	9.18 (4.037)	-3.36 (5.719)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	12.55 (7.018)	
			95% CI for LS Mean Difference [2]	-3.31, 28.41	
			p-value MMRM [2]	0.1072	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.95	
			95% CI for SMD (Hedges' g)	-0.32, 2.22	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Emotional Functioning by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
US	Week 24	Self-report	n (%)	4 (50.00)	1 (25.00)
		Parent Report	n (%)	4 (50.00)	3 (75.00)
		Absolute value	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	79.38 (23.970)	61.25 (26.575)
		Change from Baseline	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	11.68 (6.343)	-3.36 (8.977)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	15.05 (11.003)	
			95% CI for LS Mean Difference [2]	-9.53, 39.62	
			p-value MMRM [2]	0.2019	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.74	
			95% CI for SMD (Hedges' g)	-0.51, 1.98	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Emotional Functioning by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Baseline	Self-report	n (%)	6 (50.00)	3 (60.00)
		Parent Report	n (%)	5 (41.67)	2 (40.00)
		Absolute value	n (%)	11 (91.67)	5 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	65.45 (23.287)	70.00 (25.739)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Emotional Functioning by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Week 12	Self-report	n (%)	6 (50.00)	3 (60.00)
		Parent Report	n (%)	5 (41.67)	0 (0.00)
		Absolute value	n (%)	11 (91.67)	3 (60.00)
			Number of patients with missing data: n (%)	1 (8.33)	2 (40.00)
			Mean (SD)	67.73 (19.022)	68.33 (27.538)
		Change from Baseline	n (%)	11 (91.67)	3 (60.00)
			Number of patients with missing data: n (%)	1 (8.33)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	0.47 (5.557)	-5.26 (9.746)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	5.73 (11.285)	
			95% CI for LS Mean Difference [2]	-18.56, 30.01	
			p-value MMRM [2]	0.6201	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.28	
			95% CI for SMD (Hedges' g)	-1.00, 1.57	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Emotional Functioning by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Week 24	Self-report	n (%)	5 (41.67)	3 (60.00)
		Parent Report	n (%)	4 (33.33)	1 (20.00)
		Absolute value	n (%)	9 (75.00)	4 (80.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (20.00)
			Mean (SD)	73.89 (15.366)	70.00 (24.833)
		Change from Baseline	n (%)	9 (75.00)	4 (80.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	7.87 (4.663)	-2.05 (7.385)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	9.91 (8.846)	
			95% CI for LS Mean Difference [2]	-9.48, 29.31	
			p-value MMRM [2]	0.2857	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.63	
			95% CI for SMD (Hedges' g)	-0.58, 1.83	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.15.8 Pediatric Quality of Life Inventory (PEDSQL) - Emotional Functioning by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.9830	
I	Baseline	Self-report	n (%)	5 (55.56)	4 (100.00)
		Parent Report	n (%)	3 (33.33)	0 (0.00)
		Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	74.38 (22.747)	70.00 (21.985)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Program: t-qs-cont-sub.sas

Pediatric Quality of Life Inventory (PEDSQL) - Emotional Functioning by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
I	Week 12	Self-report	n (%)	5 (55.56)	3 (75.00)
		Parent Report	n (%)	3 (33.33)	1 (25.00)
		Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	69.38 (21.454)	58.75 (8.539)
		Change from Baseline	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-4.59 (5.034)	-13.32 (7.125)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	8.74 (8.733)	
			95% CI for LS Mean Difference [2]	-10.87, 28.35	
			p-value MMRM [2]	0.3420	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.54	
			95% CI for SMD (Hedges' g)	-0.69, 1.76	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Emotional Functioning by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
I	Week 24	Self-report	n (%)	5 (55.56)	3 (75.00)
		Parent Report	n (%)	3 (33.33)	1 (25.00)
		Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	78.75 (14.820)	63.75 (29.262)
		Change from Baseline	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	4.79 (5.296)	-8.32 (7.495)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	13.11 (9.185)	
			95% CI for LS Mean Difference [2]	-7.49, 33.71	
			p-value MMRM [2]	0.1853	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.76	
			95% CI for SMD (Hedges' g)	-0.48, 2.01	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Emotional Functioning by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Baseline	Self-report	n (%)	5 (45.45)	1 (20.00)
		Parent Report	n (%)	6 (54.55)	4 (80.00)
		Absolute value	n (%)	11 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	60.91 (24.064)	64.00 (21.622)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Emotional Functioning by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Week 12	Self-report	n (%)	5 (45.45)	1 (20.00)
		Parent Report	n (%)	6 (54.55)	2 (40.00)
		Absolute value	n (%)	11 (100.00)	3 (60.00)
			Number of patients with missing data: n (%)	0 (0.00)	2 (40.00)
			Mean (SD)	73.18 (20.769)	71.67 (24.664)
		Change from Baseline	n (%)	11 (100.00)	3 (60.00)
			Number of patients with missing data: n (%)	0 (0.00)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	11.26 (4.750)	4.61 (8.246)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	6.65 (9.572)	
			95% CI for LS Mean Difference [2]	-14.03, 27.34	
			p-value MMRM [2]	0.4992	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.39	
			95% CI for SMD (Hedges' g)	-0.90, 1.67	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Emotional Functioning by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Week 24	Self-report	n (%)	4 (36.36)	1 (20.00)
		Parent Report	n (%)	5 (45.45)	3 (60.00)
		Absolute value	n (%)	9 (81.82)	4 (80.00)
			Number of patients with missing data: n (%)	2 (18.18)	1 (20.00)
			Mean (SD)	74.44 (23.511)	67.50 (22.546)
		Change from Baseline	n (%)	9 (81.82)	4 (80.00)
			Number of patients with missing data: n (%)	2 (18.18)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	13.29 (5.513)	1.96 (8.855)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	11.33 (10.493)	
			95% CI for LS Mean Difference [2]	-11.54, 34.20	
			p-value MMRM [2]	0.3015	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.61	
			95% CI for SMD (Hedges' g)	-0.60, 1.81	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.15.9 Pediatric Quality of Life Inventory (PEDSQL) - Social Functioning by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.1204	
Male	Baseline	Self-report	n (%)	7 (58.33)	2 (40.00)
		Parent Report	n (%)	4 (33.33)	3 (60.00)
		Absolute value	n (%)	11 (91.67)	5 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	84.09 (16.706)	60.00 (19.685)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Social Functioning by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Male	Week 12	Self-report	n (%)	7 (58.33)	1 (20.00)
		Parent Report	n (%)	4 (33.33)	3 (60.00)
		Absolute value	n (%)	11 (91.67)	4 (80.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (20.00)
			Mean (SD)	79.09 (19.470)	56.25 (10.308)
		Change from Baseline	n (%)	11 (91.67)	4 (80.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	-1.29 (4.868)	-17.21 (8.167)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	15.92 (9.738)	
			95% CI for LS Mean Difference [2]	-5.05, 36.89	
			p-value MMRM [2]	0.1254	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.89	
			95% CI for SMD (Hedges' g)	-0.30, 2.09	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Social Functioning by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Male	Week 24	Self-report	n (%)	6 (50.00)	1 (20.00)
		Parent Report	n (%)	3 (25.00)	4 (80.00)
		Absolute value	n (%)	9 (75.00)	5 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			Mean (SD)	82.59 (14.934)	55.00 (21.794)
		Change from Baseline	n (%)	9 (75.00)	5 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	2.96 (5.444)	-15.88 (7.711)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	18.85 (9.697)	
			95% CI for LS Mean Difference [2]	-2.15, 39.85	
			p-value MMRM [2]	0.0744	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.02	
			95% CI for SMD (Hedges' g)	-0.15, 2.19	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Social Functioning by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Baseline	Self-report	n (%)	3 (37.50)	3 (75.00)
		Parent Report	n (%)	5 (62.50)	1 (25.00)
		Absolute value	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	72.50 (18.898)	66.25 (28.687)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Social Functioning by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Week 12	Self-report	n (%)	3 (37.50)	3 (75.00)
		Parent Report	n (%)	5 (62.50)	0 (0.00)
		Absolute value	n (%)	8 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			Mean (SD)	68.13 (27.247)	75.00 (31.225)
		Change from Baseline	n (%)	8 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	-4.46 (6.874)	1.88 (11.225)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-6.34 (13.162)	
			95% CI for LS Mean Difference [2]	-36.69, 24.02	
			p-value MMRM [2]	0.6431	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.28	
			95% CI for SMD (Hedges' g)	-1.61, 1.06	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Social Functioning by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Week 24	Self-report	n (%)	3 (37.50)	3 (75.00)
		Parent Report	n (%)	5 (62.50)	0 (0.00)
		Absolute value	n (%)	8 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			Mean (SD)	75.63 (18.792)	78.33 (20.207)
		Change from Baseline	n (%)	8 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	3.04 (3.862)	5.21 (6.307)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-2.17 (7.396)	
			95% CI for LS Mean Difference [2]	-19.32, 14.98	
			p-value MMRM [2]	0.7770	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.17	
			95% CI for SMD (Hedges' g)	-1.50, 1.16	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.15.10 Pediatric Quality of Life Inventory (PEDSQL) - Social Functioning by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.0701	
<10.5 years old at screening	Baseline	Self-report	n (%)	3 (25.00)	1 (25.00)
		Parent Report	n (%)	8 (66.67)	3 (75.00)
		Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	76.82 (17.787)	57.50 (15.546)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Social Functioning by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
<10.5 years old at screening	Week 12	Self-report	n (%)	3 (25.00)	0 (0.00)
		Parent Report	n (%)	8 (66.67)	3 (75.00)
		Absolute value	n (%)	11 (91.67)	3 (75.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (25.00)
			Mean (SD)	77.73 (21.721)	56.67 (12.583)
		Change from Baseline	n (%)	11 (91.67)	3 (75.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	1.12 (4.625)	-10.13 (9.126)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	11.25 (10.290)	
			95% CI for LS Mean Difference [2]	-11.15, 33.66	
			p-value MMRM [2]	0.2955	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.65	
			95% CI for SMD (Hedges' g)	-0.65, 1.96	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Social Functioning by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
<10.5 years old at screening	Week 24	Self-report	n (%)	3 (25.00)	0 (0.00)
		Parent Report	n (%)	6 (50.00)	3 (75.00)
		Absolute value	n (%)	9 (75.00)	3 (75.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
			Mean (SD)	83.33 (13.919)	51.67 (30.139)
		Change from Baseline	n (%)	9 (75.00)	3 (75.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	3.38 (4.120)	-15.13 (7.292)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	18.51 (8.640)	
			95% CI for LS Mean Difference [2]	-0.52, 37.54	
			p-value MMRM [2]	0.0555	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.32	
			95% CI for SMD (Hedges' g)	-0.11, 2.75	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Social Functioning by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Baseline	Self-report	n (%)	7 (87.50)	4 (80.00)
		Parent Report	n (%)	1 (12.50)	1 (20.00)
		Absolute value	n (%)	8 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	82.50 (19.272)	67.00 (28.196)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Social Functioning by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Week 12	Self-report	n (%)	7 (87.50)	4 (80.00)
		Parent Report	n (%)	1 (12.50)	0 (0.00)
		Absolute value	n (%)	8 (100.00)	4 (80.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (20.00)
			Mean (SD)	70.00 (25.495)	70.00 (27.386)
		Change from Baseline	n (%)	8 (100.00)	4 (80.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	-8.40 (7.334)	-4.87 (10.363)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-3.53 (12.797)	
			95% CI for LS Mean Difference [2]	-32.58, 25.53	
			p-value MMRM [2]	0.7892	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.15	
			95% CI for SMD (Hedges' g)	-1.35, 1.06	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Social Functioning by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Week 24	Self-report	n (%)	6 (75.00)	4 (80.00)
		Parent Report	n (%)	2 (25.00)	1 (20.00)
		Absolute value	n (%)	8 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	74.79 (19.282)	71.00 (17.464)
		Change from Baseline	n (%)	8 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.09 (5.261)	-0.85 (6.824)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.94 (8.560)	
			95% CI for LS Mean Difference [2]	-18.06, 19.94	
			p-value MMRM [2]	0.9145	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.06	
			95% CI for SMD (Hedges' g)	-1.06, 1.17	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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4.10.15.11 Pediatric Quality of Life Inventory (PEDSQL) - Social Functioning by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.3748	
US	Baseline	Self-report	n (%)	4 (50.00)	2 (50.00)
		Parent Report	n (%)	4 (50.00)	2 (50.00)
		Absolute value	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	85.63 (16.784)	71.25 (23.229)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Social Functioning by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
US	Week 12	Self-report	n (%)	4 (50.00)	1 (25.00)
		Parent Report	n (%)	4 (50.00)	3 (75.00)
		Absolute value	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	85.00 (25.071)	67.50 (23.979)
		Change from Baseline	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-0.93 (4.681)	-5.64 (6.695)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	4.71 (8.290)	
			95% CI for LS Mean Difference [2]	-13.75, 23.17	
			p-value MMRM [2]	0.5826	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.31	
			95% CI for SMD (Hedges' g)	-0.90, 1.52	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Social Functioning by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
US	Week 24	Self-report	n (%)	4 (50.00)	1 (25.00)
		Parent Report	n (%)	4 (50.00)	3 (75.00)
		Absolute value	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	85.00 (13.093)	63.75 (34.490)
		Change from Baseline	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-0.93 (4.428)	-9.39 (6.341)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	8.46 (7.861)	
			95% CI for LS Mean Difference [2]	-9.07, 25.98	
			p-value MMRM [2]	0.3074	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.59	
			95% CI for SMD (Hedges' g)	-0.64, 1.82	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Social Functioning by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Baseline	Self-report	n (%)	6 (50.00)	3 (60.00)
		Parent Report	n (%)	5 (41.67)	2 (40.00)
		Absolute value	n (%)	11 (91.67)	5 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	74.55 (18.365)	56.00 (22.192)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Social Functioning by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Week 12	Self-report	n (%)	6 (50.00)	3 (60.00)
		Parent Report	n (%)	5 (41.67)	0 (0.00)
		Absolute value	n (%)	11 (91.67)	3 (60.00)
			Number of patients with missing data: n (%)	1 (8.33)	2 (40.00)
			Mean (SD)	66.82 (19.010)	60.00 (22.913)
		Change from Baseline	n (%)	11 (91.67)	3 (60.00)
			Number of patients with missing data: n (%)	1 (8.33)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-4.27 (5.488)	-8.75 (10.274)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	4.49 (11.757)	
			95% CI for LS Mean Difference [2]	-20.90, 29.87	
			p-value MMRM [2]	0.7089	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.22	
			95% CI for SMD (Hedges' g)	-1.06, 1.50	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Social Functioning by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Week 24	Self-report	n (%)	5 (41.67)	3 (60.00)
		Parent Report	n (%)	4 (33.33)	1 (20.00)
		Absolute value	n (%)	9 (75.00)	4 (80.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (20.00)
			Mean (SD)	74.26 (18.618)	63.75 (7.500)
		Change from Baseline	n (%)	9 (75.00)	4 (80.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	4.35 (4.712)	-3.57 (7.449)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	7.92 (8.770)	
			95% CI for LS Mean Difference [2]	-11.23, 27.07	
			p-value MMRM [2]	0.3846	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.50	
			95% CI for SMD (Hedges' g)	-0.70, 1.69	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.15.12 Pediatric Quality of Life Inventory (PEDSQL) - Social Functioning by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.2934	
I	Baseline	Self-report	n (%)	5 (55.56)	4 (100.00)
		Parent Report	n (%)	3 (33.33)	0 (0.00)
		Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	89.38 (12.374)	68.75 (26.575)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Social Functioning by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
I	Week 12	Self-report	n (%)	5 (55.56)	3 (75.00)
		Parent Report	n (%)	3 (33.33)	1 (25.00)
		Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	82.50 (18.127)	67.50 (29.580)
		Change from Baseline	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-6.25 (4.551)	-5.00 (6.756)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.25 (8.647)	
			95% CI for LS Mean Difference [2]	-21.13, 18.63	
			p-value MMRM [2]	0.8885	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.08	
			95% CI for SMD (Hedges' g)	-1.28, 1.12	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Social Functioning by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
I	Week 24	Self-report	n (%)	5 (55.56)	3 (75.00)
		Parent Report	n (%)	3 (33.33)	1 (25.00)
		Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	82.29 (13.510)	72.50 (20.207)
		Change from Baseline	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-6.46 (4.713)	0.00 (6.974)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-6.46 (8.903)	
			95% CI for LS Mean Difference [2]	-27.02, 14.10	
			p-value MMRM [2]	0.4890	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.40	
			95% CI for SMD (Hedges' g)	-1.61, 0.81	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Social Functioning by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Baseline	Self-report	n (%)	5 (45.45)	1 (20.00)
		Parent Report	n (%)	6 (54.55)	4 (80.00)
		Absolute value	n (%)	11 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	71.82 (18.476)	58.00 (20.797)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Social Functioning by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Week 12	Self-report	n (%)	5 (45.45)	1 (20.00)
		Parent Report	n (%)	6 (54.55)	2 (40.00)
		Absolute value	n (%)	11 (100.00)	3 (60.00)
			Number of patients with missing data: n (%)	0 (0.00)	2 (40.00)
			Mean (SD)	68.64 (25.208)	60.00 (8.660)
		Change from Baseline	n (%)	11 (100.00)	3 (60.00)
			Number of patients with missing data: n (%)	0 (0.00)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-1.52 (6.252)	-6.79 (12.068)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	5.27 (13.619)	
			95% CI for LS Mean Difference [2]	-24.40, 34.93	
			p-value MMRM [2]	0.7057	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.23	
			95% CI for SMD (Hedges' g)	-1.05, 1.51	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Social Functioning by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Week 24	Self-report	n (%)	4 (36.36)	1 (20.00)
		Parent Report	n (%)	5 (45.45)	3 (60.00)
		Absolute value	n (%)	9 (81.82)	4 (80.00)
			Number of patients with missing data: n (%)	2 (18.18)	1 (20.00)
			Mean (SD)	76.67 (19.526)	55.00 (25.166)
		Change from Baseline	n (%)	9 (81.82)	4 (80.00)
			Number of patients with missing data: n (%)	2 (18.18)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	9.00 (5.651)	-9.91 (8.505)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	18.91 (10.135)	
			95% CI for LS Mean Difference [2]	-3.48, 41.30	
			p-value MMRM [2]	0.0898	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.99	
			95% CI for SMD (Hedges' g)	-0.26, 2.24	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.15.13 Pediatric Quality of Life Inventory (PEDSQL) - School Functioning by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.8991	
Male	Baseline	Self-report	n (%)	7 (58.33)	2 (40.00)
		Parent Report	n (%)	4 (33.33)	3 (60.00)
		Absolute value	n (%)	11 (91.67)	5 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	68.94 (24.748)	48.00 (18.908)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 12 parent reports, at Week 12 14 self-reports and 11 parent reports, at Week 24 13 self-reports and 11 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - School Functioning by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Male	Week 12	Self-report	n (%)	7 (58.33)	1 (20.00)
		Parent Report	n (%)	4 (33.33)	3 (60.00)
		Absolute value	n (%)	11 (91.67)	4 (80.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (20.00)
			Mean (SD)	64.55 (22.300)	63.75 (18.875)
		Change from Baseline	n (%)	11 (91.67)	4 (80.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	-3.27 (4.167)	4.56 (7.046)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-7.83 (8.289)	
			95% CI for LS Mean Difference [2]	-25.77, 10.11	
			p-value MMRM [2]	0.3621	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.51	
			95% CI for SMD (Hedges' g)	-1.67, 0.65	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 12 parent reports, at Week 12 14 self-reports and 11 parent reports, at Week 24 13 self-reports and 11 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - School Functioning by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Male	Week 24	Self-report	n (%)	6 (50.00)	1 (20.00)
		Parent Report	n (%)	3 (25.00)	4 (80.00)
		Absolute value	n (%)	9 (75.00)	5 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			Mean (SD)	67.22 (19.543)	42.00 (8.367)
		Change from Baseline	n (%)	9 (75.00)	5 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-4.94 (4.595)	-14.66 (6.378)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	9.72 (8.255)	
			95% CI for LS Mean Difference [2]	-7.94, 27.38	
			p-value MMRM [2]	0.2581	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.63	
			95% CI for SMD (Hedges' g)	-0.49, 1.76	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 12 parent reports, at Week 12 14 self-reports and 11 parent reports, at Week 24 13 self-reports and 11 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - School Functioning by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Baseline	Self-report	n (%)	3 (37.50)	3 (75.00)
		Parent Report	n (%)	4 (50.00)	1 (25.00)
		Absolute value	n (%)	7 (87.50)	4 (100.00)
			Number of patients with missing data: n (%)	1 (12.50)	0 (0.00)
			Mean (SD)	80.23 (14.049)	62.50 (21.794)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 12 parent reports, at Week 12 14 self-reports and 11 parent reports, at Week 24 13 self-reports and 11 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - School Functioning by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Week 12	Self-report	n (%)	3 (37.50)	3 (75.00)
		Parent Report	n (%)	4 (50.00)	0 (0.00)
		Absolute value	n (%)	7 (87.50)	3 (75.00)
			Number of patients with missing data: n (%)	1 (12.50)	1 (25.00)
			Mean (SD)	73.81 (18.072)	70.00 (26.458)
		Change from Baseline	n (%)	7 (87.50)	3 (75.00)
			Number of patients with missing data: n (%)	1 (12.50)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	-6.53 (4.156)	1.92 (6.504)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-8.45 (7.910)	
			95% CI for LS Mean Difference [2]	-26.86, 9.95	
			p-value MMRM [2]	0.3179	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.64	
			95% CI for SMD (Hedges' g)	-2.03, 0.75	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 12 parent reports, at Week 12 14 self-reports and 11 parent reports, at Week 24 13 self-reports and 11 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - School Functioning by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Week 24	Self-report	n (%)	3 (37.50)	3 (75.00)
		Parent Report	n (%)	4 (50.00)	0 (0.00)
		Absolute value	n (%)	7 (87.50)	3 (75.00)
			Number of patients with missing data: n (%)	1 (12.50)	1 (25.00)
			Mean (SD)	71.67 (18.709)	65.00 (30.414)
		Change from Baseline	n (%)	7 (87.50)	3 (75.00)
			Number of patients with missing data: n (%)	1 (12.50)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	-8.67 (6.253)	-3.08 (9.657)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-5.60 (11.635)	
			95% CI for LS Mean Difference [2]	-32.29, 21.09	
			p-value MMRM [2]	0.6430	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.29	
			95% CI for SMD (Hedges' g)	-1.65, 1.07	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 12 parent reports, at Week 12 14 self-reports and 11 parent reports, at Week 24 13 self-reports and 11 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.15.14 Pediatric Quality of Life Inventory (PEDSQL) - School Functioning by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.6883	
<10.5 years old at screening	Baseline	Self-report	n (%)	3 (25.00)	1 (25.00)
		Parent Report	n (%)	7 (58.33)	3 (75.00)
		Absolute value	n (%)	10 (83.33)	4 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	75.99 (21.589)	47.50 (16.583)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 12 parent reports, at Week 12 14 self-reports and 11 parent reports, at Week 24 13 self-reports and 11 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - School Functioning by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
<10.5 years old at screening	Week 12	Self-report	n (%)	3 (25.00)	0 (0.00)
		Parent Report	n (%)	7 (58.33)	3 (75.00)
		Absolute value	n (%)	10 (83.33)	3 (75.00)
			Number of patients with missing data: n (%)	2 (16.67)	1 (25.00)
			Mean (SD)	71.67 (21.943)	65.00 (22.913)
		Change from Baseline	n (%)	10 (83.33)	3 (75.00)
			Number of patients with missing data: n (%)	2 (16.67)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	-3.68 (2.893)	9.33 (5.537)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-13.01 (6.408)	
			95% CI for LS Mean Difference [2]	-27.10, 1.08	
			p-value MMRM [2]	0.0670	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-1.25	
			95% CI for SMD (Hedges' g)	-2.64, 0.14	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 12 parent reports, at Week 12 14 self-reports and 11 parent reports, at Week 24 13 self-reports and 11 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - School Functioning by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
<10.5 years old at screening	Week 24	Self-report	n (%)	3 (25.00)	0 (0.00)
		Parent Report	n (%)	5 (41.67)	3 (75.00)
		Absolute value	n (%)	8 (66.67)	3 (75.00)
			Number of patients with missing data: n (%)	4 (33.33)	1 (25.00)
			Mean (SD)	72.71 (23.787)	40.00 (5.000)
		Change from Baseline	n (%)	8 (66.67)	3 (75.00)
			Number of patients with missing data: n (%)	4 (33.33)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	-4.06 (5.501)	-15.67 (8.935)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	11.61 (10.666)	
			95% CI for LS Mean Difference [2]	-12.34, 35.56	
			p-value MMRM [2]	0.3034	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.65	
			95% CI for SMD (Hedges' g)	-0.71, 2.01	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 12 parent reports, at Week 12 14 self-reports and 11 parent reports, at Week 24 13 self-reports and 11 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - School Functioning by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Baseline	Self-report	n (%)	7 (87.50)	4 (80.00)
		Parent Report	n (%)	1 (12.50)	1 (20.00)
		Absolute value	n (%)	8 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	70.00 (22.361)	60.00 (23.184)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 12 parent reports, at Week 12 14 self-reports and 11 parent reports, at Week 24 13 self-reports and 11 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - School Functioning by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Week 12	Self-report	n (%)	7 (87.50)	4 (80.00)
		Parent Report	n (%)	1 (12.50)	0 (0.00)
		Absolute value	n (%)	8 (100.00)	4 (80.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (20.00)
			Mean (SD)	63.75 (19.594)	67.50 (22.174)
		Change from Baseline	n (%)	8 (100.00)	4 (80.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	-6.10 (5.231)	-1.42 (7.206)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-4.67 (8.916)	
			95% CI for LS Mean Difference [2]	-24.39, 15.04	
			p-value MMRM [2]	0.6109	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.28	
			95% CI for SMD (Hedges' g)	-1.49, 0.93	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 12 parent reports, at Week 12 14 self-reports and 11 parent reports, at Week 24 13 self-reports and 11 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - School Functioning by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Week 24	Self-report	n (%)	6 (75.00)	4 (80.00)
		Parent Report	n (%)	2 (25.00)	1 (20.00)
		Absolute value	n (%)	8 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	65.63 (12.374)	57.00 (25.150)
		Change from Baseline	n (%)	8 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-8.08 (5.366)	-6.67 (6.845)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.41 (8.961)	
			95% CI for LS Mean Difference [2]	-20.91, 18.08	
			p-value MMRM [2]	0.8772	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.08	
			95% CI for SMD (Hedges' g)	-1.20, 1.03	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 12 parent reports, at Week 12 14 self-reports and 11 parent reports, at Week 24 13 self-reports and 11 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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4.10.15.15 Pediatric Quality of Life Inventory (PEDSQL) - School Functioning by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.3862	
US	Baseline	Self-report	n (%)	4 (50.00)	2 (50.00)
		Parent Report	n (%)	3 (37.50)	2 (50.00)
		Absolute value	n (%)	7 (87.50)	4 (100.00)
			Number of patients with missing data: n (%)	1 (12.50)	0 (0.00)
			Mean (SD)	80.71 (14.268)	58.75 (26.575)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 12 parent reports, at Week 12 14 self-reports and 11 parent reports, at Week 24 13 self-reports and 11 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - School Functioning by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
US	Week 12	Self-report	n (%)	4 (50.00)	1 (25.00)
		Parent Report	n (%)	3 (37.50)	3 (75.00)
		Absolute value	n (%)	7 (87.50)	4 (100.00)
			Number of patients with missing data: n (%)	1 (12.50)	0 (0.00)
			Mean (SD)	80.00 (17.559)	71.25 (22.500)
		Change from Baseline	n (%)	7 (87.50)	4 (100.00)
			Number of patients with missing data: n (%)	1 (12.50)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.70 (4.866)	6.28 (6.635)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-5.58 (8.639)	
			95% CI for LS Mean Difference [2]	-25.16, 14.00	
			p-value MMRM [2]	0.5346	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.37	
			95% CI for SMD (Hedges' g)	-1.61, 0.87	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 12 parent reports, at Week 12 14 self-reports and 11 parent reports, at Week 24 13 self-reports and 11 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - School Functioning by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
US	Week 24	Self-report	n (%)	4 (50.00)	1 (25.00)
		Parent Report	n (%)	3 (37.50)	3 (75.00)
		Absolute value	n (%)	7 (87.50)	4 (100.00)
			Number of patients with missing data: n (%)	1 (12.50)	0 (0.00)
			Mean (SD)	77.14 (17.995)	50.00 (20.412)
		Change from Baseline	n (%)	7 (87.50)	4 (100.00)
			Number of patients with missing data: n (%)	1 (12.50)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-2.16 (5.323)	-14.97 (7.223)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	12.81 (9.350)	
			95% CI for LS Mean Difference [2]	-8.24, 33.86	
			p-value MMRM [2]	0.2028	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.78	
			95% CI for SMD (Hedges' g)	-0.50, 2.06	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 12 parent reports, at Week 12 14 self-reports and 11 parent reports, at Week 24 13 self-reports and 11 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - School Functioning by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Baseline	Self-report	n (%)	6 (50.00)	3 (60.00)
		Parent Report	n (%)	5 (41.67)	2 (40.00)
		Absolute value	n (%)	11 (91.67)	5 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	68.63 (24.511)	51.00 (16.355)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 12 parent reports, at Week 12 14 self-reports and 11 parent reports, at Week 24 13 self-reports and 11 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - School Functioning by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Week 12	Self-report	n (%)	6 (50.00)	3 (60.00)
		Parent Report	n (%)	5 (41.67)	0 (0.00)
		Absolute value	n (%)	11 (91.67)	3 (60.00)
			Number of patients with missing data: n (%)	1 (8.33)	2 (40.00)
			Mean (SD)	60.61 (19.597)	60.00 (20.000)
		Change from Baseline	n (%)	11 (91.67)	3 (60.00)
			Number of patients with missing data: n (%)	1 (8.33)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-7.60 (3.447)	-2.31 (6.760)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-5.29 (7.618)	
			95% CI for LS Mean Difference [2]	-21.95, 11.38	
			p-value MMRM [2]	0.5013	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.41	
			95% CI for SMD (Hedges' g)	-1.70, 0.88	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 12 parent reports, at Week 12 14 self-reports and 11 parent reports, at Week 24 13 self-reports and 11 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - School Functioning by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Week 24	Self-report	n (%)	5 (41.67)	3 (60.00)
		Parent Report	n (%)	4 (33.33)	1 (20.00)
		Absolute value	n (%)	9 (75.00)	4 (80.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (20.00)
			Mean (SD)	62.96 (17.674)	51.25 (24.958)
		Change from Baseline	n (%)	9 (75.00)	4 (80.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	-9.50 (5.217)	-5.85 (7.901)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-3.65 (9.698)	
			95% CI for LS Mean Difference [2]	-24.66, 17.36	
			p-value MMRM [2]	0.7129	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.21	
			95% CI for SMD (Hedges' g)	-1.39, 0.97	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 12 parent reports, at Week 12 14 self-reports and 11 parent reports, at Week 24 13 self-reports and 11 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.15.16 Pediatric Quality of Life Inventory (PEDSQL) - School Functioning by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.7630	
I	Baseline	Self-report	n (%)	5 (55.56)	4 (100.00)
		Parent Report	n (%)	2 (22.22)	0 (0.00)
		Absolute value	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	84.51 (11.846)	62.50 (21.794)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 12 parent reports, at Week 12 14 self-reports and 11 parent reports, at Week 24 13 self-reports and 11 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - School Functioning by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
I	Week 12	Self-report	n (%)	5 (55.56)	3 (75.00)
		Parent Report	n (%)	2 (22.22)	1 (25.00)
		Absolute value	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	73.81 (15.596)	67.50 (22.174)
		Change from Baseline	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-10.22 (5.558)	0.40 (7.778)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-10.63 (10.420)	
			95% CI for LS Mean Difference [2]	-34.55, 13.30	
			p-value MMRM [2]	0.3369	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.60	
			95% CI for SMD (Hedges' g)	-1.86, 0.66	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 12 parent reports, at Week 12 14 self-reports and 11 parent reports, at Week 24 13 self-reports and 11 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - School Functioning by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
I	Week 24	Self-report	n (%)	5 (55.56)	3 (75.00)
		Parent Report	n (%)	2 (22.22)	1 (25.00)
		Absolute value	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			Mean (SD)	71.67 (18.930)	60.00 (26.771)
		Change from Baseline	n (%)	7 (77.78)	4 (100.00)
			Number of patients with missing data: n (%)	2 (22.22)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-12.36 (6.455)	-7.10 (8.908)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-5.27 (11.756)	
			95% CI for LS Mean Difference [2]	-31.73, 21.19	
			p-value MMRM [2]	0.6643	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.26	
			95% CI for SMD (Hedges' g)	-1.50, 0.97	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 12 parent reports, at Week 12 14 self-reports and 11 parent reports, at Week 24 13 self-reports and 11 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - School Functioning by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Baseline	Self-report	n (%)	5 (45.45)	1 (20.00)
		Parent Report	n (%)	6 (54.55)	4 (80.00)
		Absolute value	n (%)	11 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	66.21 (23.620)	48.00 (18.908)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 12 parent reports, at Week 12 14 self-reports and 11 parent reports, at Week 24 13 self-reports and 11 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - School Functioning by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Week 12	Self-report	n (%)	5 (45.45)	1 (20.00)
		Parent Report	n (%)	6 (54.55)	2 (40.00)
		Absolute value	n (%)	11 (100.00)	3 (60.00)
			Number of patients with missing data: n (%)	0 (0.00)	2 (40.00)
			Mean (SD)	64.55 (23.394)	65.00 (22.913)
		Change from Baseline	n (%)	11 (100.00)	3 (60.00)
			Number of patients with missing data: n (%)	0 (0.00)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-1.18 (3.698)	7.76 (7.306)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-8.94 (8.228)	
			95% CI for LS Mean Difference [2]	-27.04, 9.17	
			p-value MMRM [2]	0.3005	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.64	
			95% CI for SMD (Hedges' g)	-1.95, 0.66	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 12 parent reports, at Week 12 14 self-reports and 11 parent reports, at Week 24 13 self-reports and 11 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - School Functioning by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Week 24	Self-report	n (%)	4 (36.36)	1 (20.00)
		Parent Report	n (%)	5 (45.45)	3 (60.00)
		Absolute value	n (%)	9 (81.82)	4 (80.00)
			Number of patients with missing data: n (%)	2 (18.18)	1 (20.00)
			Mean (SD)	67.22 (19.383)	41.25 (9.465)
		Change from Baseline	n (%)	9 (81.82)	4 (80.00)
			Number of patients with missing data: n (%)	2 (18.18)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	-2.62 (4.897)	-11.22 (7.381)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	8.60 (9.099)	
			95% CI for LS Mean Difference [2]	-11.29, 28.49	
			p-value MMRM [2]	0.3637	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.52	
			95% CI for SMD (Hedges' g)	-0.68, 1.72	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 12 parent reports, at Week 12 14 self-reports and 11 parent reports, at Week 24 13 self-reports and 11 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.15.17 Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.9035	
Male	Baseline	Self-report	n (%)	7 (58.33)	2 (40.00)
		Parent Report	n (%)	4 (33.33)	3 (60.00)
		Absolute value	n (%)	11 (91.67)	5 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	75.20 (17.380)	55.22 (18.691)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Male	Week 12	Self-report	n (%)	7 (58.33)	1 (20.00)
		Parent Report	n (%)	4 (33.33)	3 (60.00)
		Absolute value	n (%)	11 (91.67)	4 (80.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (20.00)
			Mean (SD)	70.47 (16.150)	56.52 (8.420)
		Change from Baseline	n (%)	11 (91.67)	4 (80.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	-2.64 (3.247)	-10.80 (5.374)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	8.16 (6.433)	
			95% CI for LS Mean Difference [2]	-5.91, 22.23	
			p-value MMRM [2]	0.2296	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.68	
			95% CI for SMD (Hedges' g)	-0.50, 1.85	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Male	Week 24	Self-report	n (%)	6 (50.00)	1 (20.00)
		Parent Report	n (%)	4 (33.33)	4 (80.00)
		Absolute value	n (%)	10 (83.33)	5 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			Mean (SD)	75.30 (12.527)	51.74 (6.857)
		Change from Baseline	n (%)	10 (83.33)	5 (100.00)
			Number of patients with missing data: n (%)	2 (16.67)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.86 (3.069)	-13.88 (4.740)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	14.74 (5.910)	
			95% CI for LS Mean Difference [2]	1.88, 27.60	
			p-value MMRM [2]	0.0280 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.33	
			95% CI for SMD (Hedges' g)	0.14, 2.52	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Baseline	Self-report	n (%)	3 (37.50)	3 (75.00)
		Parent Report	n (%)	5 (62.50)	1 (25.00)
		Absolute value	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	68.73 (14.219)	72.83 (20.335)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Week 12	Self-report	n (%)	3 (37.50)	3 (75.00)
		Parent Report	n (%)	5 (62.50)	1 (25.00)
		Absolute value	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	66.36 (21.194)	65.49 (19.932)
		Change from Baseline	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-2.20 (5.526)	-7.59 (7.816)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	5.40 (9.594)	
			95% CI for LS Mean Difference [2]	-16.16, 26.95	
			p-value MMRM [2]	0.5870	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.30	
			95% CI for SMD (Hedges' g)	-0.91, 1.51	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Week 24	Self-report	n (%)	3 (37.50)	3 (75.00)
		Parent Report	n (%)	5 (62.50)	0 (0.00)
		Absolute value	n (%)	8 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			Mean (SD)	71.87 (18.769)	70.29 (25.196)
		Change from Baseline	n (%)	8 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	3.31 (3.685)	-7.88 (5.724)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	11.19 (6.861)	
			95% CI for LS Mean Difference [2]	-4.21, 26.59	
			p-value MMRM [2]	0.1357	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.94	
			95% CI for SMD (Hedges' g)	-0.46, 2.33	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.15.18 Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.0140 ***	
<10.5 years old at screening	Baseline	Self-report	n (%)	3 (25.00)	1 (25.00)
		Parent Report	n (%)	8 (66.67)	3 (75.00)
		Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	71.93 (14.864)	58.42 (11.719)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
<10.5 years old at screening	Week 12	Self-report	n (%)	3 (25.00)	0 (0.00)
		Parent Report	n (%)	8 (66.67)	4 (100.00)
		Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	70.81 (18.842)	52.99 (9.491)
		Change from Baseline	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-0.27 (4.120)	-11.72 (6.940)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	11.45 (8.164)	
			95% CI for LS Mean Difference [2]	-6.17, 29.07	
			p-value MMRM [2]	0.1841	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.76	
			95% CI for SMD (Hedges' g)	-0.43, 1.94	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
<10.5 years old at screening	Week 24	Self-report	n (%)	3 (25.00)	0 (0.00)
		Parent Report	n (%)	7 (58.33)	3 (75.00)
		Absolute value	n (%)	10 (83.33)	3 (75.00)
			Number of patients with missing data: n (%)	2 (16.67)	1 (25.00)
			Mean (SD)	78.56 (14.548)	50.00 (4.981)
		Change from Baseline	n (%)	10 (83.33)	3 (75.00)
			Number of patients with missing data: n (%)	2 (16.67)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	6.86 (2.980)	-15.72 (5.435)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	22.59 (6.319)	
			95% CI for LS Mean Difference [2]	8.75, 36.43	
			p-value MMRM [2]	0.0041 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	2.14	
			95% CI for SMD (Hedges' g)	0.57, 3.70	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Baseline	Self-report	n (%)	7 (87.50)	4 (80.00)
		Parent Report	n (%)	1 (12.50)	1 (20.00)
		Absolute value	n (%)	8 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	73.23 (18.564)	66.74 (26.274)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Week 12	Self-report	n (%)	7 (87.50)	4 (80.00)
		Parent Report	n (%)	1 (12.50)	0 (0.00)
		Absolute value	n (%)	8 (100.00)	4 (80.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (20.00)
			Mean (SD)	65.90 (17.603)	69.02 (16.134)
		Change from Baseline	n (%)	8 (100.00)	4 (80.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	-7.17 (3.658)	-4.46 (4.942)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-2.71 (6.154)	
			95% CI for LS Mean Difference [2]	-16.38, 10.96	
			p-value MMRM [2]	0.6685	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.23	
			95% CI for SMD (Hedges' g)	-1.44, 0.97	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Week 24	Self-report	n (%)	6 (75.00)	4 (80.00)
		Parent Report	n (%)	2 (25.00)	1 (20.00)
		Absolute value	n (%)	8 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	67.79 (14.689)	63.91 (20.558)
		Change from Baseline	n (%)	8 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-6.08 (3.550)	-4.87 (4.563)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-1.21 (5.819)	
			95% CI for LS Mean Difference [2]	-14.13, 11.71	
			p-value MMRM [2]	0.8394	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.11	
			95% CI for SMD (Hedges' g)	-1.22, 1.01	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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4.10.15.19 Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.6428	
US	Baseline	Self-report	n (%)	4 (50.00)	2 (50.00)
		Parent Report	n (%)	4 (50.00)	2 (50.00)
		Absolute value	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	77.09 (13.629)	65.49 (20.592)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
US	Week 12	Self-report	n (%)	4 (50.00)	1 (25.00)
		Parent Report	n (%)	4 (50.00)	3 (75.00)
		Absolute value	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	75.11 (18.139)	63.59 (18.221)
		Change from Baseline	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-2.07 (3.836)	-5.54 (5.483)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.48 (6.787)	
			95% CI for LS Mean Difference [2]	-11.73, 18.69	
			p-value MMRM [2]	0.6199	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.28	
			95% CI for SMD (Hedges' g)	-0.93, 1.49	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
US	Week 24	Self-report	n (%)	4 (50.00)	1 (25.00)
		Parent Report	n (%)	4 (50.00)	3 (75.00)
		Absolute value	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	79.16 (16.178)	60.87 (22.116)
		Change from Baseline	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	1.99 (3.530)	-8.26 (5.056)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	10.25 (6.270)	
			95% CI for LS Mean Difference [2]	-3.88, 24.37	
			p-value MMRM [2]	0.1357	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.89	
			95% CI for SMD (Hedges' g)	-0.37, 2.15	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Baseline	Self-report	n (%)	6 (50.00)	3 (60.00)
		Parent Report	n (%)	5 (41.67)	2 (40.00)
		Absolute value	n (%)	11 (91.67)	5 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	69.12 (17.421)	61.09 (22.427)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Week 12	Self-report	n (%)	6 (50.00)	3 (60.00)
		Parent Report	n (%)	5 (41.67)	1 (20.00)
		Absolute value	n (%)	11 (91.67)	4 (80.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (20.00)
			Mean (SD)	64.11 (17.225)	58.42 (13.115)
		Change from Baseline	n (%)	11 (91.67)	4 (80.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	-4.47 (3.905)	-8.88 (6.307)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	4.41 (7.435)	
			95% CI for LS Mean Difference [2]	-11.61, 20.43	
			p-value MMRM [2]	0.5626	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.31	
			95% CI for SMD (Hedges' g)	-0.84, 1.46	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Week 24	Self-report	n (%)	5 (41.67)	3 (60.00)
		Parent Report	n (%)	5 (41.67)	1 (20.00)
		Absolute value	n (%)	10 (83.33)	4 (80.00)
			Number of patients with missing data: n (%)	2 (16.67)	1 (20.00)
			Mean (SD)	69.47 (13.667)	56.52 (14.116)
		Change from Baseline	n (%)	10 (83.33)	4 (80.00)
			Number of patients with missing data: n (%)	2 (16.67)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	0.12 (3.337)	-9.63 (5.309)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	9.74 (6.324)	
			95% CI for LS Mean Difference [2]	-3.96, 23.45	
			p-value MMRM [2]	0.1481	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.83	
			95% CI for SMD (Hedges' g)	-0.37, 2.04	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.15.20 Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.2703	
I	Baseline	Self-report	n (%)	5 (55.56)	4 (100.00)
		Parent Report	n (%)	3 (33.33)	0 (0.00)
		Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	84.49 (10.641)	69.02 (23.888)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
I	Week 12	Self-report	n (%)	5 (55.56)	3 (75.00)
		Parent Report	n (%)	3 (33.33)	1 (25.00)
		Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	73.96 (16.678)	68.48 (16.580)
		Change from Baseline	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-10.17 (3.952)	-5.06 (5.742)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-5.11 (7.214)	
			95% CI for LS Mean Difference [2]	-21.27, 11.05	
			p-value MMRM [2]	0.4954	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.40	
			95% CI for SMD (Hedges' g)	-1.61, 0.82	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
I	Week 24	Self-report	n (%)	5 (55.56)	3 (75.00)
		Parent Report	n (%)	3 (33.33)	1 (25.00)
		Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	78.56 (12.780)	65.49 (22.703)
		Change from Baseline	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-5.57 (3.854)	-8.05 (5.607)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.49 (7.053)	
			95% CI for LS Mean Difference [2]	-13.35, 18.32	
			p-value MMRM [2]	0.7322	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.20	
			95% CI for SMD (Hedges' g)	-1.01, 1.40	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Baseline	Self-report	n (%)	5 (45.45)	1 (20.00)
		Parent Report	n (%)	6 (54.55)	4 (80.00)
		Absolute value	n (%)	11 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	63.74 (13.579)	58.26 (18.424)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Week 12	Self-report	n (%)	5 (45.45)	1 (20.00)
		Parent Report	n (%)	6 (54.55)	3 (60.00)
		Absolute value	n (%)	11 (100.00)	4 (80.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (20.00)
			Mean (SD)	64.94 (18.729)	53.53 (9.898)
		Change from Baseline	n (%)	11 (100.00)	4 (80.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	1.48 (3.993)	-8.51 (6.402)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	9.99 (7.556)	
			95% CI for LS Mean Difference [2]	-6.41, 26.38	
			p-value MMRM [2]	0.2100	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.68	
			95% CI for SMD (Hedges' g)	-0.49, 1.86	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Week 24	Self-report	n (%)	4 (36.36)	1 (20.00)
		Parent Report	n (%)	6 (54.55)	3 (60.00)
		Absolute value	n (%)	10 (90.91)	4 (80.00)
			Number of patients with missing data: n (%)	1 (9.09)	1 (20.00)
			Mean (SD)	69.94 (16.522)	51.90 (7.907)
		Change from Baseline	n (%)	10 (90.91)	4 (80.00)
			Number of patients with missing data: n (%)	1 (9.09)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	5.61 (3.651)	-8.89 (5.783)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	14.50 (6.886)	
			95% CI for LS Mean Difference [2]	-0.42, 29.43	
			p-value MMRM [2]	0.0559	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.13	
			95% CI for SMD (Hedges' g)	-0.11, 2.38	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.15.21 Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score responders ≥ 15 by gender

Gender	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	Interaction	Treatment*Gender, p-value Chi-Square[1]	0.9658	
Male	Week 12	n (%)	12 (100.00)	5 (71.43)
		Self-report: n (%)	7 (58.33)	1 (14.29)
		Parent Report: n (%)	4 (33.33)	3 (42.86)
		Number of patients with missing data: n (%)	0 (0.00)	2 (28.57)
		Number of patients imputed as non-responders: n (%)	1 (8.33)	1 (14.29)
		Non-Responders [1]	10 (83.33)	5 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	2.62 (0.11, 64.69)	
		RR (95% CI)	2.31 (0.13, 41.03)	
		RD % (95% CI)	10.90 (-19.89, 41.69)	
		p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score responders ≥ 15 by gender

Gender	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Male	Week 24	n (%)	12 (100.00)	5 (71.43)
		Self-report: n (%)	6 (50.00)	1 (14.29)
		Parent Report: n (%)	4 (33.33)	4 (57.14)
		Number of patients with missing data: n (%)	0 (0.00)	2 (28.57)
		Number of patients imputed as non-responders: n (%)	2 (16.67)	0 (0.00)
		Non-Responders [1]	11 (91.67)	4 (80.00)
		Responders	1 (8.33)	1 (20.00)
		OR (95% CI)	0.36 (0.02, 7.29)	
		RR (95% CI)	0.42 (0.03, 5.43)	
		RD % (95% CI)	-11.67 (-50.06, 26.72)	
		p-value – Fisher's Exact Test	0.5147	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Table Generation: 11SEP2023 12:07:21 PM
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Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score responders ≥ 15 by gender

Gender	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Week 12	n (%)	8 (88.89)	4 (100.00)
		Self-report: n (%)	3 (33.33)	3 (75.00)
		Parent Report: n (%)	5 (55.56)	1 (25.00)
		Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
		Number of patients imputed as non-responders: n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	7 (87.50)	4 (100.00)
		Responders	1 (12.50)	0 (0.00)
		OR (95% CI)	1.80 (0.06, 54.33)	
		RR (95% CI)	1.67 (0.08, 33.75)	
		RD % (95% CI)	6.67 (-29.17, 42.50)	
		p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score responders ≥ 15 by gender

Gender	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Week 24	n (%)	8 (88.89)	4 (100.00)
		Self-report: n (%)	3 (33.33)	3 (75.00)
		Parent Report: n (%)	5 (55.56)	0 (0.00)
		Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
		Number of patients imputed as non-responders: n (%)	0 (0.00)	1 (25.00)
		Non-Responders [1]	5 (62.50)	4 (100.00)
		Responders	3 (37.50)	0 (0.00)
		OR (95% CI)	5.73 (0.23, 142.55)	
		RR (95% CI)	3.89 (0.25, 61.09)	
		RD % (95% CI)	28.89 (-12.41, 70.19)	
		p-value – Fisher's Exact Test	0.4909	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.15.22 Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score responders ≥ 15 by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	Interaction	Treatment*Age Group, p-value Chi-Square[1]	0.9506	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Self-report: n (%)	3 (25.00)	0 (0.00)
		Parent Report: n (%)	8 (66.67)	4 (100.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders: n (%)	1 (8.33)	0 (0.00)
		Non-Responders [1]	10 (83.33)	4 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	2.14 (0.08, 54.22)	
		RR (95% CI)	1.92 (0.11, 33.44)	
		RD % (95% CI)	9.23 (-24.69, 43.15)	
		p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
Program: t-qs-categ-pedsql-sub.sas
Table Generation: 11SEP2023 12:07:28 PM

Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score responders ≥ 15 by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
<10.5 years old at screening	Week 24	n (%)	12 (100.00)	4 (100.00)
		Self-report: n (%)	3 (25.00)	0 (0.00)
		Parent Report: n (%)	7 (58.33)	3 (75.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders: n (%)	2 (16.67)	1 (25.00)
		Non-Responders [1]	8 (66.67)	4 (100.00)
		Responders	4 (33.33)	0 (0.00)
		OR (95% CI)	4.76 (0.21, 109.78)	
		RR (95% CI)	3.46 (0.22, 53.27)	
		RD % (95% CI)	24.62 (-12.27, 61.50)	
		p-value – Fisher's Exact Test	0.5165	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
Program: t-qs-categ-pedsql-sub.sas
Table Generation: 11SEP2023 12:07:28 PM

Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score responders ≥ 15 by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	8 (88.89)	5 (71.43)
		Self-report: n (%)	7 (77.78)	4 (57.14)
		Parent Report: n (%)	1 (11.11)	0 (0.00)
		Number of patients with missing data: n (%)	1 (11.11)	2 (28.57)
		Number of patients imputed as non-responders: n (%)	0 (0.00)	1 (14.29)
		Non-Responders [1]	7 (87.50)	5 (100.00)
		Responders	1 (12.50)	0 (0.00)
		OR (95% CI)	2.20 (0.07, 64.90)	
		RR (95% CI)	2.00 (0.10, 41.37)	
		RD % (95% CI)	8.33 (-24.56, 41.23)	
		p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
Program: t-qs-categ-pedsql-sub.sas
Table Generation: 11SEP2023 12:07:28 PM

Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score responders ≥ 15 by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Week 24	n (%)	8 (88.89)	5 (71.43)
		Self-report: n (%)	6 (66.67)	4 (57.14)
		Parent Report: n (%)	2 (22.22)	1 (14.29)
		Number of patients with missing data: n (%)	1 (11.11)	2 (28.57)
		Number of patients imputed as non-responders: n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	8 (100.00)	4 (80.00)
		Responders	0 (0.00)	1 (20.00)
		OR (95% CI)	0.18 (0.01, 5.28)	
		RR (95% CI)	0.22 (0.01, 4.60)	
		RD % (95% CI)	-19.44 (-57.19, 18.30)	
		p-value – Fisher's Exact Test	0.3846	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
Program: t-qs-categ-pedsql-sub.sas
Table Generation: 11SEP2023 12:07:28 PM

4.10.15.23 Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score responders ≥ 15 by region

Region	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	Interaction	Treatment*Region, p-value Chi-Square[1]	0.9693	
US	Week 12	n (%)	8 (100.00)	4 (66.67)
		Self-report: n (%)	4 (50.00)	1 (16.67)
		Parent Report: n (%)	4 (50.00)	3 (50.00)
		Number of patients with missing data: n (%)	0 (0.00)	2 (33.33)
		Number of patients imputed as non-responders: n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	7 (87.50)	4 (100.00)
		Responders	1 (12.50)	0 (0.00)
		OR (95% CI)	1.80 (0.06, 54.33)	
		RR (95% CI)	1.67 (0.08, 33.75)	
		RD % (95% CI)	6.67 (-29.17, 42.50)	
		p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Table Generation: 11SEP2023 12:07:35 PM
Program: t-qs-categ-pedsql-sub.sas

Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score responders ≥ 15 by region

Region	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
US	Week 24	n (%)	8 (100.00)	4 (66.67)
		Self-report: n (%)	4 (50.00)	1 (16.67)
		Parent Report: n (%)	4 (50.00)	3 (50.00)
		Number of patients with missing data: n (%)	0 (0.00)	2 (33.33)
		Number of patients imputed as non-responders: n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	6 (75.00)	4 (100.00)
		Responders	2 (25.00)	0 (0.00)
		OR (95% CI)	3.46 (0.13, 90.68)	
		RR (95% CI)	2.78 (0.16, 47.20)	
		RD % (95% CI)	17.78 (-21.56, 57.12)	
		p-value – Fisher's Exact Test	0.5152	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Table Generation: 11SEP2023 12:07:35 PM
Program: t-qs-categ-pedsql-sub.sas

Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score responders ≥ 15 by region

Region	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Week 12	n (%)	12 (92.31)	5 (100.00)
		Self-report: n (%)	6 (46.15)	3 (60.00)
		Parent Report: n (%)	5 (38.46)	1 (20.00)
		Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
		Number of patients imputed as non-responders: n (%)	1 (7.69)	1 (20.00)
		Non-Responders [1]	10 (83.33)	5 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	2.62 (0.11, 64.69)	
		RR (95% CI)	2.31 (0.13, 41.03)	
		RD % (95% CI)	10.90 (-19.89, 41.69)	
		p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Table Generation: 11SEP2023 12:07:35 PM
Program: t-qs-categ-pedsql-sub.sas

Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score responders ≥ 15 by region

Region	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Week 24	n (%)	12 (92.31)	5 (100.00)
		Self-report: n (%)	5 (38.46)	3 (60.00)
		Parent Report: n (%)	5 (38.46)	1 (20.00)
		Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
		Number of patients imputed as non-responders: n (%)	2 (15.38)	1 (20.00)
		Non-Responders [1]	10 (83.33)	4 (80.00)
		Responders	2 (16.67)	1 (20.00)
		OR (95% CI)	0.80 (0.06, 11.50)	
		RR (95% CI)	0.83 (0.10, 7.24)	
		RD % (95% CI)	-3.33 (-44.25, 37.58)	
		p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Table Generation: 11SEP2023 12:07:35 PM
Program: t-qs-categ-pedsql-sub.sas

4.10.15.24 Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score responders ≥ 15 by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	Interaction	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.9982	
I	Week 12	n (%)	9 (100.00)	4 (80.00)
		Self-report: n (%)	5 (55.56)	3 (60.00)
		Parent Report: n (%)	3 (33.33)	1 (20.00)
		Number of patients with missing data: n (%)	0 (0.00)	1 (20.00)
		Number of patients imputed as non-responders: n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	9 (100.00)	4 (100.00)
	Week 24	n (%)	9 (100.00)	4 (80.00)
		Self-report: n (%)	5 (55.56)	3 (60.00)
		Parent Report: n (%)	3 (33.33)	1 (20.00)
		Number of patients with missing data: n (%)	0 (0.00)	1 (20.00)
		Number of patients imputed as non-responders: n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	9 (100.00)	4 (100.00)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Table Generation: 11SEP2023 12:07:42 PM
Program: t-qs-categ-pedsql-sub.sas

Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score responders ≥ 15 by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Week 12	n (%)	11 (91.67)	5 (83.33)
		Self-report: n (%)	5 (41.67)	1 (16.67)
		Parent Report: n (%)	6 (50.00)	3 (50.00)
		Number of patients with missing data: n (%)	1 (8.33)	1 (16.67)
		Number of patients imputed as non-responders: n (%)	0 (0.00)	1 (16.67)
		Non-Responders [1]	8 (72.73)	5 (100.00)
		Responders	3 (27.27)	0 (0.00)
		OR (95% CI)	4.53 (0.19, 105.84)	
		RR (95% CI)	3.50 (0.21, 57.35)	
		RD % (95% CI)	20.83 (-13.08, 54.75)	
		p-value – Fisher's Exact Test	0.5089	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Table Generation: 11SEP2023 12:07:42 PM
Program: t-qs-categ-pedsql-sub.sas

Pediatric Quality of Life Inventory (PEDSQL) - Total Scale Score responders ≥ 15 by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Week 24	n (%)	11 (91.67)	5 (83.33)
		Self-report: n (%)	4 (33.33)	1 (16.67)
		Parent Report: n (%)	6 (50.00)	3 (50.00)
		Number of patients with missing data: n (%)	1 (8.33)	1 (16.67)
		Number of patients imputed as non-responders: n (%)	1 (8.33)	1 (16.67)
		Non-Responders [1]	7 (63.64)	4 (80.00)
		Responders	4 (36.36)	1 (20.00)
		OR (95% CI)	2.29 (0.19, 28.19)	
		RR (95% CI)	1.82 (0.27, 12.39)	
		RD % (95% CI)	16.36 (-28.77, 61.50)	
		p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 13 parent reports, at Week 24 13 self-reports and 13 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Table Generation: 11SEP2023 12:07:42 PM
Program: t-qs-categ-pedsql-sub.sas

4.10.15.25 Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.2098	
Male	Baseline	Self-report	n (%)	7 (58.33)	2 (40.00)
		Parent Report	n (%)	4 (33.33)	3 (60.00)
		Absolute value	n (%)	11 (91.67)	5 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	73.01 (25.048)	51.88 (21.148)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
Table Generation: 11SEP2023 1:34:53 PM
Program: t-qs-cont-sub.sas

Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Male	Week 12	Self-report	n (%)	7 (58.33)	1 (20.00)
		Parent Report	n (%)	4 (33.33)	3 (60.00)
		Absolute value	n (%)	11 (91.67)	4 (80.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (20.00)
			Mean (SD)	65.34 (24.506)	44.53 (13.592)
		Change from Baseline	n (%)	11 (91.67)	4 (80.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	-5.86 (5.749)	-24.95 (9.547)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	19.09 (11.235)	
			95% CI for LS Mean Difference [2]	-5.79, 43.97	
			p-value MMRM [2]	0.1188	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.88	
			95% CI for SMD (Hedges' g)	-0.31, 2.08	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
Table Generation: 11SEP2023 1:34:53 PM
Program: t-qs-cont-sub.sas

Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Male	Week 24	Self-report	n (%)	6 (50.00)	1 (20.00)
		Parent Report	n (%)	3 (25.00)	4 (80.00)
		Absolute value	n (%)	9 (75.00)	5 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			Mean (SD)	75.00 (21.819)	49.38 (10.680)
		Change from Baseline	n (%)	9 (75.00)	5 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	1.04 (6.808)	-16.73 (9.430)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	17.77 (12.016)	
			95% CI for LS Mean Difference [2]	-8.96, 44.50	
			p-value MMRM [2]	0.1696	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.76	
			95% CI for SMD (Hedges' g)	-0.38, 1.89	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
Table Generation: 11SEP2023 1:34:53 PM
Program: t-qs-cont-sub.sas

Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Baseline	Self-report	n (%)	3 (37.50)	3 (75.00)
		Parent Report	n (%)	5 (62.50)	1 (25.00)
		Absolute value	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	69.53 (22.654)	84.39 (23.112)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Week 12	Self-report	n (%)	3 (37.50)	3 (75.00)
		Parent Report	n (%)	5 (62.50)	0 (0.00)
		Absolute value	n (%)	8 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			Mean (SD)	62.49 (24.191)	80.21 (13.002)
		Change from Baseline	n (%)	8 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	-8.95 (7.845)	4.05 (12.974)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-13.00 (15.327)	
			95% CI for LS Mean Difference [2]	-48.07, 22.06	
			p-value MMRM [2]	0.4198	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.50	
			95% CI for SMD (Hedges' g)	-1.85, 0.85	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Week 24	Self-report	n (%)	3 (37.50)	3 (75.00)
		Parent Report	n (%)	5 (62.50)	0 (0.00)
		Absolute value	n (%)	8 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			Mean (SD)	67.71 (21.465)	65.62 (21.875)
		Change from Baseline	n (%)	8 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	-3.73 (7.125)	-10.54 (11.814)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	6.81 (13.977)	
			95% CI for LS Mean Difference [2]	-25.36, 38.98	
			p-value MMRM [2]	0.6391	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.29	
			95% CI for SMD (Hedges' g)	-1.05, 1.62	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.15.26 Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.3423	
<10.5 years old at screening	Baseline	Self-report	n (%)	3 (25.00)	1 (25.00)
		Parent Report	n (%)	8 (66.67)	3 (75.00)
		Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	74.71 (19.991)	67.97 (20.786)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
<10.5 years old at screening	Week 12	Self-report	n (%)	3 (25.00)	0 (0.00)
		Parent Report	n (%)	8 (66.67)	3 (75.00)
		Absolute value	n (%)	11 (91.67)	3 (75.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (25.00)
			Mean (SD)	64.77 (26.437)	46.88 (15.625)
		Change from Baseline	n (%)	11 (91.67)	3 (75.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	-7.55 (7.833)	-25.93 (15.012)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	18.38 (16.992)	
			95% CI for LS Mean Difference [2]	-19.20, 55.96	
			p-value MMRM [2]	0.3034	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.63	
			95% CI for SMD (Hedges' g)	-0.67, 1.93	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
<10.5 years old at screening	Week 24	Self-report	n (%)	3 (25.00)	0 (0.00)
		Parent Report	n (%)	6 (50.00)	3 (75.00)
		Absolute value	n (%)	9 (75.00)	3 (75.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
			Mean (SD)	80.33 (18.075)	56.25 (5.413)
		Change from Baseline	n (%)	9 (75.00)	3 (75.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	6.94 (5.711)	-16.56 (10.260)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	23.50 (11.783)	
			95% CI for LS Mean Difference [2]	-3.17, 50.17	
			p-value MMRM [2]	0.0774	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.19	
			95% CI for SMD (Hedges' g)	-0.22, 2.59	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Baseline	Self-report	n (%)	7 (87.50)	4 (80.00)
		Parent Report	n (%)	1 (12.50)	1 (20.00)
		Absolute value	n (%)	8 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	67.19 (28.446)	65.01 (33.259)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Week 12	Self-report	n (%)	7 (87.50)	4 (80.00)
		Parent Report	n (%)	1 (12.50)	0 (0.00)
		Absolute value	n (%)	8 (100.00)	4 (80.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (20.00)
			Mean (SD)	63.28 (21.179)	69.53 (23.848)
		Change from Baseline	n (%)	8 (100.00)	4 (80.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	-5.74 (5.312)	-3.60 (7.166)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-2.13 (8.908)	
			95% CI for LS Mean Difference [2]	-22.55, 18.28	
			p-value MMRM [2]	0.8164	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.12	
			95% CI for SMD (Hedges' g)	-1.32, 1.08	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Week 24	Self-report	n (%)	6 (75.00)	4 (80.00)
		Parent Report	n (%)	2 (25.00)	1 (20.00)
		Absolute value	n (%)	8 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	61.72 (21.311)	55.00 (21.483)
		Change from Baseline	n (%)	8 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-9.82 (5.694)	-13.14 (7.221)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.33 (9.240)	
			95% CI for LS Mean Difference [2]	-17.31, 23.96	
			p-value MMRM [2]	0.7266	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.18	
			95% CI for SMD (Hedges' g)	-0.94, 1.30	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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4.10.15.27 Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.9446	
US	Baseline	Self-report	n (%)	4 (50.00)	2 (50.00)
		Parent Report	n (%)	4 (50.00)	2 (50.00)
		Absolute value	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	75.79 (22.085)	67.98 (20.807)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
US	Week 12	Self-report	n (%)	4 (50.00)	1 (25.00)
		Parent Report	n (%)	4 (50.00)	3 (75.00)
		Absolute value	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	67.19 (24.206)	57.81 (25.312)
		Change from Baseline	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-8.35 (7.457)	-16.91 (10.548)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	8.56 (12.921)	
			95% CI for LS Mean Difference [2]	-20.68, 37.81	
			p-value MMRM [2]	0.5241	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.35	
			95% CI for SMD (Hedges' g)	-0.86, 1.56	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
US	Week 24	Self-report	n (%)	4 (50.00)	1 (25.00)
		Parent Report	n (%)	4 (50.00)	3 (75.00)
		Absolute value	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	75.78 (21.698)	64.06 (16.238)
		Change from Baseline	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	0.24 (6.570)	-10.66 (9.295)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	10.90 (11.387)	
			95% CI for LS Mean Difference [2]	-14.86, 36.66	
			p-value MMRM [2]	0.3634	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.51	
			95% CI for SMD (Hedges' g)	-0.71, 1.73	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Baseline	Self-report	n (%)	6 (50.00)	3 (60.00)
		Parent Report	n (%)	5 (41.67)	2 (40.00)
		Absolute value	n (%)	11 (91.67)	5 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	68.46 (25.020)	65.00 (33.249)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Week 12	Self-report	n (%)	6 (50.00)	3 (60.00)
		Parent Report	n (%)	5 (41.67)	0 (0.00)
		Absolute value	n (%)	11 (91.67)	3 (60.00)
			Number of patients with missing data: n (%)	1 (8.33)	2 (40.00)
			Mean (SD)	61.92 (24.309)	62.51 (23.605)
		Change from Baseline	n (%)	11 (91.67)	3 (60.00)
			Number of patients with missing data: n (%)	1 (8.33)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-6.13 (6.659)	-6.72 (12.599)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.58 (14.256)	
			95% CI for LS Mean Difference [2]	-30.57, 31.73	
			p-value MMRM [2]	0.9680	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.02	
			95% CI for SMD (Hedges' g)	-1.25, 1.30	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Week 24	Self-report	n (%)	5 (41.67)	3 (60.00)
		Parent Report	n (%)	4 (33.33)	1 (20.00)
		Absolute value	n (%)	9 (75.00)	4 (80.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (20.00)
			Mean (SD)	67.83 (21.492)	46.88 (13.239)
		Change from Baseline	n (%)	9 (75.00)	4 (80.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	-1.86 (6.643)	-18.68 (10.165)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	16.82 (12.288)	
			95% CI for LS Mean Difference [2]	-10.61, 44.24	
			p-value MMRM [2]	0.2015	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.74	
			95% CI for SMD (Hedges' g)	-0.48, 1.96	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.15.28 Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.4654	
I	Baseline	Self-report	n (%)	5 (55.56)	4 (100.00)
		Parent Report	n (%)	3 (33.33)	0 (0.00)
		Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	88.68 (11.568)	72.67 (28.122)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Program: t-qs-cont-sub.sas

Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
I	Week 12	Self-report	n (%)	5 (55.56)	3 (75.00)
		Parent Report	n (%)	3 (33.33)	1 (25.00)
		Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	73.44 (20.044)	75.78 (13.824)
		Change from Baseline	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-13.24 (6.438)	-7.12 (9.259)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-6.13 (11.526)	
			95% CI for LS Mean Difference [2]	-32.05, 19.79	
			p-value MMRM [2]	0.6072	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.29	
			95% CI for SMD (Hedges' g)	-1.50, 0.92	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
Table Generation: 11SEP2023 1:35:11 PM
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
I	Week 24	Self-report	n (%)	5 (55.56)	3 (75.00)
		Parent Report	n (%)	3 (33.33)	1 (25.00)
		Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	79.30 (16.697)	64.06 (18.131)
		Change from Baseline	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-7.39 (6.119)	-18.84 (8.816)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	11.45 (10.993)	
			95% CI for LS Mean Difference [2]	-13.37, 36.28	
			p-value MMRM [2]	0.3243	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.57	
			95% CI for SMD (Hedges' g)	-0.66, 1.80	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Baseline	Self-report	n (%)	5 (45.45)	1 (20.00)
		Parent Report	n (%)	6 (54.55)	4 (80.00)
		Absolute value	n (%)	11 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	59.09 (22.206)	61.25 (27.740)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Week 12	Self-report	n (%)	5 (45.45)	1 (20.00)
		Parent Report	n (%)	6 (54.55)	2 (40.00)
		Absolute value	n (%)	11 (100.00)	3 (60.00)
			Number of patients with missing data: n (%)	0 (0.00)	2 (40.00)
			Mean (SD)	57.38 (24.763)	38.54 (7.867)
		Change from Baseline	n (%)	11 (100.00)	3 (60.00)
			Number of patients with missing data: n (%)	0 (0.00)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-1.57 (6.499)	-22.45 (12.256)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	20.89 (13.872)	
			95% CI for LS Mean Difference [2]	-9.40, 51.18	
			p-value MMRM [2]	0.1585	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.87	
			95% CI for SMD (Hedges' g)	-0.46, 2.19	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Week 24	Self-report	n (%)	4 (36.36)	1 (20.00)
		Parent Report	n (%)	5 (45.45)	3 (60.00)
		Absolute value	n (%)	9 (81.82)	4 (80.00)
			Number of patients with missing data: n (%)	2 (18.18)	1 (20.00)
			Mean (SD)	64.70 (23.465)	46.88 (10.508)
		Change from Baseline	n (%)	9 (81.82)	4 (80.00)
			Number of patients with missing data: n (%)	2 (18.18)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	4.84 (7.185)	-10.86 (10.924)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	15.70 (13.155)	
			95% CI for LS Mean Difference [2]	-13.69, 45.09	
			p-value MMRM [2]	0.2607	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.64	
			95% CI for SMD (Hedges' g)	-0.57, 1.85	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.15.29 Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score responders ≥ 15 by gender

Gender	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	Interaction	Treatment*Gender, p-value Chi-Square[1]	0.9772	
Male	Week 12	n (%)	12 (100.00)	5 (71.43)
		Self-report: n (%)	7 (58.33)	1 (14.29)
		Parent Report: n (%)	4 (33.33)	3 (42.86)
		Number of patients with missing data: n (%)	0 (0.00)	2 (28.57)
		Number of patients imputed as non-responders: n (%)	1 (8.33)	1 (14.29)
		Non-Responders [1]	10 (83.33)	5 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	2.62 (0.11, 64.69)	
		RR (95% CI)	2.31 (0.13, 41.03)	
		RD % (95% CI)	10.90 (-19.89, 41.69)	
		p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score responders ≥ 15 by gender

Gender	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Male	Week 24	n (%)	12 (100.00)	5 (71.43)
		Self-report: n (%)	6 (50.00)	1 (14.29)
		Parent Report: n (%)	3 (25.00)	4 (57.14)
		Number of patients with missing data: n (%)	0 (0.00)	2 (28.57)
		Number of patients imputed as non-responders: n (%)	3 (25.00)	0 (0.00)
		Non-Responders [1]	9 (75.00)	4 (80.00)
		Responders	3 (25.00)	1 (20.00)
		OR (95% CI)	1.33 (0.10, 17.10)	
		RR (95% CI)	1.25 (0.17, 9.31)	
		RD % (95% CI)	5.00 (-37.77, 47.77)	
		p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Table Generation: 11SEP2023 12:07:48 PM
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score responders ≥ 15 by gender

Gender	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Week 12	n (%)	8 (88.89)	4 (100.00)
		Self-report: n (%)	3 (33.33)	3 (75.00)
		Parent Report: n (%)	5 (55.56)	0 (0.00)
		Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
		Number of patients imputed as non-responders: n (%)	0 (0.00)	1 (25.00)
		Non-Responders [1]	6 (75.00)	3 (75.00)
		Responders	2 (25.00)	1 (25.00)
		OR (95% CI)	1.00 (0.06, 15.99)	
		RR (95% CI)	1.00 (0.13, 8.00)	
		RD % (95% CI)	0.00 (-51.97, 51.97)	
		p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score responders ≥ 15 by gender

Gender	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Week 24	n (%)	8 (88.89)	4 (100.00)
		Self-report: n (%)	3 (33.33)	3 (75.00)
		Parent Report: n (%)	5 (55.56)	0 (0.00)
		Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
		Number of patients imputed as non-responders: n (%)	0 (0.00)	1 (25.00)
		Non-Responders [1]	5 (62.50)	4 (100.00)
		Responders	3 (37.50)	0 (0.00)
		OR (95% CI)	5.73 (0.23, 142.55)	
		RR (95% CI)	3.89 (0.25, 61.09)	
		RD % (95% CI)	28.89 (-12.41, 70.19)	
		p-value – Fisher's Exact Test	0.4909	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Program: t-qs-categ-pedsql-sub.sas

4.10.15.30 Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score responders ≥ 15 by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	Interaction	Treatment*Age Group, p-value Chi-Square[1]	0.9775	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Self-report: n (%)	3 (25.00)	0 (0.00)
		Parent Report: n (%)	8 (66.67)	3 (75.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders: n (%)	1 (8.33)	1 (25.00)
		Non-Responders [1]	10 (83.33)	4 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	2.14 (0.08, 54.22)	
		RR (95% CI)	1.92 (0.11, 33.44)	
		RD % (95% CI)	9.23 (-24.69, 43.15)	
		p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score responders ≥ 15 by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
<10.5 years old at screening	Week 24	n (%)	12 (100.00)	4 (100.00)
		Self-report: n (%)	3 (25.00)	0 (0.00)
		Parent Report: n (%)	6 (50.00)	3 (75.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders: n (%)	3 (25.00)	1 (25.00)
		Non-Responders [1]	8 (66.67)	4 (100.00)
		Responders	4 (33.33)	0 (0.00)
		OR (95% CI)	4.76 (0.21, 109.78)	
		RR (95% CI)	3.46 (0.22, 53.27)	
		RD % (95% CI)	24.62 (-12.27, 61.50)	
		p-value – Fisher's Exact Test	0.5165	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
Program: t-qs-categ-pedsql-sub.sas
Table Generation: 11SEP2023 12:07:55 PM

Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score responders ≥ 15 by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Week 12	n (%)	8 (88.89)	5 (71.43)
		Self-report: n (%)	7 (77.78)	4 (57.14)
		Parent Report: n (%)	1 (11.11)	0 (0.00)
		Number of patients with missing data: n (%)	1 (11.11)	2 (28.57)
		Number of patients imputed as non-responders: n (%)	0 (0.00)	1 (14.29)
		Non-Responders [1]	6 (75.00)	4 (80.00)
		Responders	2 (25.00)	1 (20.00)
		OR (95% CI)	1.33 (0.09, 20.11)	
		RR (95% CI)	1.25 (0.15, 10.46)	
		RD % (95% CI)	5.00 (-41.15, 51.15)	
		p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
Program: t-qs-categ-pedsql-sub.sas
Table Generation: 11SEP2023 12:07:55 PM

Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score responders ≥ 15 by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Week 24	n (%)	8 (88.89)	5 (71.43)
		Self-report: n (%)	6 (66.67)	4 (57.14)
		Parent Report: n (%)	2 (22.22)	1 (14.29)
		Number of patients with missing data: n (%)	1 (11.11)	2 (28.57)
		Number of patients imputed as non-responders: n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	6 (75.00)	4 (80.00)
		Responders	2 (25.00)	1 (20.00)
		OR (95% CI)	1.33 (0.09, 20.11)	
		RR (95% CI)	1.25 (0.15, 10.46)	
		RD % (95% CI)	5.00 (-41.15, 51.15)	
		p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
Program: t-qs-categ-pedsql-sub.sas
Table Generation: 11SEP2023 12:07:55 PM

4.10.15.31 Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score responders ≥ 15 by region

Region	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	Interaction	Treatment*Region, p-value Chi-Square[1]	0.9772	
US	Week 12	n (%)	8 (100.00)	4 (66.67)
		Self-report: n (%)	4 (50.00)	1 (16.67)
		Parent Report: n (%)	4 (50.00)	3 (50.00)
		Number of patients with missing data: n (%)	0 (0.00)	2 (33.33)
		Number of patients imputed as non-responders: n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	7 (87.50)	4 (100.00)
		Responders	1 (12.50)	0 (0.00)
		OR (95% CI)	1.80 (0.06, 54.33)	
		RR (95% CI)	1.67 (0.08, 33.75)	
		RD % (95% CI)	6.67 (-29.17, 42.50)	
		p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Table Generation: 11SEP2023 12:08:02 PM
Program: t-qs-categ-pedsql-sub.sas

Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score responders ≥ 15 by region

Region	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
US	Week 24	n (%)	8 (100.00)	4 (66.67)
		Self-report: n (%)	4 (50.00)	1 (16.67)
		Parent Report: n (%)	4 (50.00)	3 (50.00)
		Number of patients with missing data: n (%)	0 (0.00)	2 (33.33)
		Number of patients imputed as non-responders: n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	5 (62.50)	4 (100.00)
		Responders	3 (37.50)	0 (0.00)
		OR (95% CI)	5.73 (0.23, 142.55)	
		RR (95% CI)	3.89 (0.25, 61.09)	
		RD % (95% CI)	28.89 (-12.41, 70.19)	
		p-value – Fisher's Exact Test	0.4909	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Table Generation: 11SEP2023 12:08:02 PM
Program: t-qs-categ-pedsql-sub.sas

Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score responders ≥ 15 by region

Region	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Week 12	n (%)	12 (92.31)	5 (100.00)
		Self-report: n (%)	6 (46.15)	3 (60.00)
		Parent Report: n (%)	5 (38.46)	0 (0.00)
		Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
		Number of patients imputed as non-responders: n (%)	1 (7.69)	2 (40.00)
		Non-Responders [1]	9 (75.00)	4 (80.00)
		Responders	3 (25.00)	1 (20.00)
		OR (95% CI)	1.33 (0.10, 17.10)	
		RR (95% CI)	1.25 (0.17, 9.31)	
		RD % (95% CI)	5.00 (-37.77, 47.77)	
		p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Table Generation: 11SEP2023 12:08:02 PM
Program: t-qs-categ-pedsql-sub.sas

Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score responders ≥ 15 by region

Region	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Week 24	n (%)	12 (92.31)	5 (100.00)
		Self-report: n (%)	5 (38.46)	3 (60.00)
		Parent Report: n (%)	4 (30.77)	1 (20.00)
		Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
		Number of patients imputed as non-responders: n (%)	3 (23.08)	1 (20.00)
		Non-Responders [1]	9 (75.00)	4 (80.00)
		Responders	3 (25.00)	1 (20.00)
		OR (95% CI)	1.33 (0.10, 17.10)	
		RR (95% CI)	1.25 (0.17, 9.31)	
		RD % (95% CI)	5.00 (-37.77, 47.77)	
		p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Table Generation: 11SEP2023 12:08:02 PM
Program: t-qs-categ-pedsql-sub.sas

4.10.15.32 Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score responders ≥ 15 by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	Interaction	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.9816	
I	Week 12	n (%)	9 (100.00)	4 (80.00)
		Self-report: n (%)	5 (55.56)	3 (60.00)
		Parent Report: n (%)	3 (33.33)	1 (20.00)
		Number of patients with missing data: n (%)	0 (0.00)	1 (20.00)
		Number of patients imputed as non-responders: n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	9 (100.00)	3 (75.00)
		Responders	0 (0.00)	1 (25.00)
		OR (95% CI)	0.12 (0.00, 3.78)	
		RR (95% CI)	0.17 (0.01, 3.40)	
		RD % (95% CI)	-25.00 (-67.38, 17.38)	
		p-value – Fisher's Exact Test	0.3077	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Table Generation: 11SEP2023 12:08:08 PM
Program: t-qs-categ-pedsql-sub.sas

Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score responders ≥ 15 by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
I	Week 24	n (%)	9 (100.00)	4 (80.00)
		Self-report: n (%)	5 (55.56)	3 (60.00)
		Parent Report: n (%)	3 (33.33)	1 (20.00)
		Number of patients with missing data: n (%)	0 (0.00)	1 (20.00)
		Number of patients imputed as non-responders: n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	8 (88.89)	4 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	1.59 (0.05, 47.52)	
		RR (95% CI)	1.50 (0.07, 30.59)	
		RD % (95% CI)	5.00 (-29.37, 39.37)	
		p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Table Generation: 11SEP2023 12:08:08 PM
Program: t-qs-categ-pedsql-sub.sas

Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score responders ≥ 15 by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Week 12	n (%)	11 (91.67)	5 (83.33)
		Self-report: n (%)	5 (41.67)	1 (16.67)
		Parent Report: n (%)	6 (50.00)	2 (33.33)
		Number of patients with missing data: n (%)	1 (8.33)	1 (16.67)
		Number of patients imputed as non-responders: n (%)	0 (0.00)	2 (33.33)
		Non-Responders [1]	7 (63.64)	5 (100.00)
		Responders	4 (36.36)	0 (0.00)
		OR (95% CI)	6.60 (0.29, 149.77)	
		RR (95% CI)	4.50 (0.29, 70.57)	
		RD % (95% CI)	29.17 (-6.04, 64.37)	
		p-value – Fisher's Exact Test	0.2445	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Table Generation: 11SEP2023 12:08:08 PM
Program: t-qs-categ-pedsql-sub.sas

Pediatric Quality of Life Inventory (PEDSQL) - Physical Health Summary Score responders ≥ 15 by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Week 24	n (%)	11 (91.67)	5 (83.33)
		Self-report: n (%)	4 (33.33)	1 (16.67)
		Parent Report: n (%)	5 (41.67)	3 (50.00)
		Number of patients with missing data: n (%)	1 (8.33)	1 (16.67)
		Number of patients imputed as non-responders: n (%)	2 (16.67)	1 (16.67)
		Non-Responders [1]	6 (54.55)	4 (80.00)
		Responders	5 (45.45)	1 (20.00)
		OR (95% CI)	3.33 (0.28, 40.29)	
		RR (95% CI)	2.27 (0.35, 14.73)	
		RD % (95% CI)	25.45 (-20.32, 71.23)	
		p-value – Fisher's Exact Test	0.5879	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Table Generation: 11SEP2023 12:08:08 PM
Program: t-qs-categ-pedsql-sub.sas

4.10.15.33 Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*Gender, p-value MMRM [1]	0.9592	
Male	Baseline	Self-report	n (%)	7 (58.33)	2 (40.00)
		Parent Report	n (%)	4 (33.33)	3 (60.00)
		Absolute value	n (%)	11 (91.67)	5 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	76.17 (16.563)	56.99 (18.808)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
Table Generation: 11SEP2023 1:35:17 PM
Program: t-qs-cont-sub.sas

Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Male	Week 12	Self-report	n (%)	7 (58.33)	1 (20.00)
		Parent Report	n (%)	4 (33.33)	3 (60.00)
		Absolute value	n (%)	11 (91.67)	4 (80.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (20.00)
			Mean (SD)	73.03 (15.327)	62.90 (11.150)
		Change from Baseline	n (%)	11 (91.67)	4 (80.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	-1.29 (3.201)	-3.72 (5.377)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	2.43 (6.399)	
			95% CI for LS Mean Difference [2]	-11.45, 16.30	
			p-value MMRM [2]	0.7108	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.21	
			95% CI for SMD (Hedges' g)	-0.94, 1.35	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
Table Generation: 11SEP2023 1:35:17 PM
Program: t-qs-cont-sub.sas

Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Male	Week 24	Self-report	n (%)	6 (50.00)	1 (20.00)
		Parent Report	n (%)	3 (25.00)	4 (80.00)
		Absolute value	n (%)	9 (75.00)	5 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			Mean (SD)	76.63 (13.035)	52.99 (12.896)
		Change from Baseline	n (%)	9 (75.00)	5 (100.00)
			Number of patients with missing data: n (%)	3 (25.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	1.23 (3.242)	-12.37 (4.747)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	13.60 (5.990)	
			95% CI for LS Mean Difference [2]	0.74, 26.45	
			p-value MMRM [2]	0.0396 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.23	
			95% CI for SMD (Hedges' g)	0.03, 2.43	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
Table Generation: 11SEP2023 1:35:17 PM
Program: t-qs-cont-sub.sas

Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Baseline	Self-report	n (%)	3 (37.50)	3 (75.00)
		Parent Report	n (%)	5 (62.50)	1 (25.00)
		Absolute value	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	67.68 (13.580)	66.68 (22.409)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Week 12	Self-report	n (%)	3 (37.50)	3 (75.00)
		Parent Report	n (%)	5 (62.50)	0 (0.00)
		Absolute value	n (%)	8 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			Mean (SD)	68.86 (20.902)	67.80 (21.122)
		Change from Baseline	n (%)	8 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	1.47 (3.927)	-6.32 (6.441)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	7.79 (7.573)	
			95% CI for LS Mean Difference [2]	-9.41, 24.99	
			p-value MMRM [2]	0.3312	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.60	
			95% CI for SMD (Hedges' g)	-0.75, 1.96	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score by gender

Gender	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Week 24	Self-report	n (%)	3 (37.50)	3 (75.00)
		Parent Report	n (%)	5 (62.50)	0 (0.00)
		Absolute value	n (%)	8 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			Mean (SD)	74.25 (18.483)	72.83 (27.019)
		Change from Baseline	n (%)	8 (100.00)	3 (75.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	6.86 (2.977)	-1.29 (4.899)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	8.14 (5.771)	
			95% CI for LS Mean Difference [2]	-5.12, 21.41	
			p-value MMRM [2]	0.1951	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.82	
			95% CI for SMD (Hedges' g)	-0.56, 2.20	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.15.34 Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*Age Group, p-value MMRM [1]	0.0163 ***	
<10.5 years old at screening	Baseline	Self-report	n (%)	3 (25.00)	1 (25.00)
		Parent Report	n (%)	8 (66.67)	3 (75.00)
		Absolute value	n (%)	11 (91.67)	4 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	69.85 (15.623)	53.34 (12.243)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
<10.5 years old at screening	Week 12	Self-report	n (%)	3 (25.00)	0 (0.00)
		Parent Report	n (%)	8 (66.67)	3 (75.00)
		Absolute value	n (%)	11 (91.67)	3 (75.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (25.00)
			Mean (SD)	74.24 (17.431)	60.00 (11.664)
		Change from Baseline	n (%)	11 (91.67)	3 (75.00)
			Number of patients with missing data: n (%)	1 (8.33)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	4.59 (2.781)	0.08 (5.467)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	4.51 (6.190)	
			95% CI for LS Mean Difference [2]	-8.97, 17.98	
			p-value MMRM [2]	0.4802	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.44	
			95% CI for SMD (Hedges' g)	-0.85, 1.73	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
<10.5 years old at screening	Week 24	Self-report	n (%)	3 (25.00)	0 (0.00)
		Parent Report	n (%)	6 (50.00)	3 (75.00)
		Absolute value	n (%)	9 (75.00)	3 (75.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
			Mean (SD)	79.60 (16.432)	46.68 (9.985)
		Change from Baseline	n (%)	9 (75.00)	3 (75.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (25.00)
			LS Mean Change from Baseline (SE) [2]	8.05 (2.538)	-13.24 (4.520)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	21.29 (5.311)	
			95% CI for LS Mean Difference [2]	9.54, 33.03	
			p-value MMRM [2]	0.0022 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	2.46	
			95% CI for SMD (Hedges' g)	0.77, 4.16	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Baseline	Self-report	n (%)	7 (87.50)	4 (80.00)
		Parent Report	n (%)	1 (12.50)	1 (20.00)
		Absolute value	n (%)	8 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	76.37 (15.723)	67.66 (23.583)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Week 12	Self-report	n (%)	7 (87.50)	4 (80.00)
		Parent Report	n (%)	1 (12.50)	0 (0.00)
		Absolute value	n (%)	8 (100.00)	4 (80.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (20.00)
			Mean (SD)	67.20 (17.809)	68.75 (17.350)
		Change from Baseline	n (%)	8 (100.00)	4 (80.00)
			Number of patients with missing data: n (%)	0 (0.00)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	-8.53 (3.624)	-5.43 (5.053)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-3.11 (6.232)	
			95% CI for LS Mean Difference [2]	-17.11, 10.90	
			p-value MMRM [2]	0.6296	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.27	
			95% CI for SMD (Hedges' g)	-1.47, 0.94	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score by age group

Age Group	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Week 24	Self-report	n (%)	6 (75.00)	4 (80.00)
		Parent Report	n (%)	2 (25.00)	1 (20.00)
		Absolute value	n (%)	8 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	70.90 (13.594)	68.68 (20.956)
		Change from Baseline	n (%)	8 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-3.76 (3.658)	-0.69 (4.731)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-3.07 (6.004)	
			95% CI for LS Mean Difference [2]	-16.38, 10.24	
			p-value MMRM [2]	0.6199	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.26	
			95% CI for SMD (Hedges' g)	-1.38, 0.86	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
NOTE: Median age used as cut-off point.
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4.10.15.35 Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*Region, p-value MMRM [1]	0.3399	
US	Baseline	Self-report	n (%)	4 (50.00)	2 (50.00)
		Parent Report	n (%)	4 (50.00)	2 (50.00)
		Absolute value	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	77.02 (14.920)	64.18 (20.652)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
US	Week 12	Self-report	n (%)	4 (50.00)	1 (25.00)
		Parent Report	n (%)	4 (50.00)	3 (75.00)
		Absolute value	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	79.71 (16.301)	66.68 (16.399)
		Change from Baseline	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	2.88 (2.296)	-0.37 (3.312)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	3.25 (4.136)	
			95% CI for LS Mean Difference [2]	-6.09, 12.59	
			p-value MMRM [2]	0.4519	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.43	
			95% CI for SMD (Hedges' g)	-0.78, 1.65	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
US	Week 24	Self-report	n (%)	4 (50.00)	1 (25.00)
		Parent Report	n (%)	4 (50.00)	3 (75.00)
		Absolute value	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	81.43 (15.151)	59.18 (26.291)
		Change from Baseline	n (%)	8 (100.00)	4 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	4.59 (3.940)	-7.87 (5.610)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	12.46 (6.917)	
			95% CI for LS Mean Difference [2]	-2.89, 27.81	
			p-value MMRM [2]	0.1009	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.98	
			95% CI for SMD (Hedges' g)	-0.29, 2.26	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Baseline	Self-report	n (%)	6 (50.00)	3 (60.00)
		Parent Report	n (%)	5 (41.67)	2 (40.00)
		Absolute value	n (%)	11 (91.67)	5 (100.00)
			Number of patients with missing data: n (%)	1 (8.33)	0 (0.00)
			Mean (SD)	69.38 (15.936)	58.99 (21.157)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Week 12	Self-report	n (%)	6 (50.00)	3 (60.00)
		Parent Report	n (%)	5 (41.67)	0 (0.00)
		Absolute value	n (%)	11 (91.67)	3 (60.00)
			Number of patients with missing data: n (%)	1 (8.33)	2 (40.00)
			Mean (SD)	65.14 (16.261)	62.77 (15.386)
		Change from Baseline	n (%)	11 (91.67)	3 (60.00)
			Number of patients with missing data: n (%)	1 (8.33)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	-3.93 (3.725)	-5.51 (6.961)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.57 (7.903)	
			95% CI for LS Mean Difference [2]	-15.54, 18.69	
			p-value MMRM [2]	0.8453	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.12	
			95% CI for SMD (Hedges' g)	-1.16, 1.39	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score by region

Region	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Week 24	Self-report	n (%)	5 (41.67)	3 (60.00)
		Parent Report	n (%)	4 (33.33)	1 (20.00)
		Absolute value	n (%)	9 (75.00)	4 (80.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (20.00)
			Mean (SD)	70.25 (14.311)	61.68 (16.094)
		Change from Baseline	n (%)	9 (75.00)	4 (80.00)
			Number of patients with missing data: n (%)	3 (25.00)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	1.30 (3.178)	-3.21 (4.961)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	4.51 (5.912)	
			95% CI for LS Mean Difference [2]	-8.46, 17.49	
			p-value MMRM [2]	0.4608	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.42	
			95% CI for SMD (Hedges' g)	-0.77, 1.61	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.15.36 Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	All	Interaction test	Treatment*GMFCS at Baseline, p-value MMRM [1]	0.4745	
I	Baseline	Self-report	n (%)	5 (55.56)	4 (100.00)
		Parent Report	n (%)	3 (33.33)	0 (0.00)
		Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	81.65 (13.755)	67.09 (21.926)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
Table Generation: 11SEP2023 1:35:36 PM
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Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
I	Week 12	Self-report	n (%)	5 (55.56)	3 (75.00)
		Parent Report	n (%)	3 (33.33)	1 (25.00)
		Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	74.73 (15.327)	64.60 (18.395)
		Change from Baseline	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-6.39 (3.414)	-6.06 (4.970)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	-0.33 (6.255)	
			95% CI for LS Mean Difference [2]	-14.48, 13.82	
			p-value MMRM [2]	0.9589	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	-0.03	
			95% CI for SMD (Hedges' g)	-1.23, 1.17	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Program: t-qs-cont-sub.sas

Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
I	Week 24	Self-report	n (%)	5 (55.56)	3 (75.00)
		Parent Report	n (%)	3 (33.33)	1 (25.00)
		Absolute value	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			Mean (SD)	78.67 (12.734)	66.29 (25.646)
		Change from Baseline	n (%)	8 (88.89)	4 (100.00)
			Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
			LS Mean Change from Baseline (SE) [2]	-2.45 (4.638)	-4.37 (6.664)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	1.92 (8.288)	
			95% CI for LS Mean Difference [2]	-16.48, 20.33	
			p-value MMRM [2]	0.8212	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.13	
			95% CI for SMD (Hedges' g)	-1.07, 1.33	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Baseline	Self-report	n (%)	5 (45.45)	1 (20.00)
		Parent Report	n (%)	6 (54.55)	4 (80.00)
		Absolute value	n (%)	11 (100.00)	5 (100.00)
			Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
			Mean (SD)	66.01 (13.822)	56.66 (19.013)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Week 12	Self-report	n (%)	5 (45.45)	1 (20.00)
		Parent Report	n (%)	6 (54.55)	2 (40.00)
		Absolute value	n (%)	11 (100.00)	3 (60.00)
			Number of patients with missing data: n (%)	0 (0.00)	2 (40.00)
			Mean (SD)	68.76 (19.179)	65.53 (12.037)
		Change from Baseline	n (%)	11 (100.00)	3 (60.00)
			Number of patients with missing data: n (%)	0 (0.00)	2 (40.00)
			LS Mean Change from Baseline (SE) [2]	2.91 (3.683)	2.42 (7.084)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	0.49 (7.989)	
			95% CI for LS Mean Difference [2]	-17.14, 18.12	
			p-value MMRM [2]	0.9523	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	0.04	
			95% CI for SMD (Hedges' g)	-1.24, 1.31	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score by GMFCS

GMFCS at Baseline	Visit	Value Category	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Week 24	Self-report	n (%)	4 (36.36)	1 (20.00)
		Parent Report	n (%)	5 (45.45)	3 (60.00)
		Absolute value	n (%)	9 (81.82)	4 (80.00)
			Number of patients with missing data: n (%)	2 (18.18)	1 (20.00)
			Mean (SD)	72.69 (17.635)	54.57 (14.322)
		Change from Baseline	n (%)	9 (81.82)	4 (80.00)
			Number of patients with missing data: n (%)	2 (18.18)	1 (20.00)
			LS Mean Change from Baseline (SE) [2]	6.97 (2.989)	-5.54 (4.582)
			LS Mean Difference (SE) (Pegzilarginase – Placebo)[2]	12.51 (5.490)	
			95% CI for LS Mean Difference [2]	0.43, 24.59	
			p-value MMRM [2]	0.0436 ***	
			SMD (Hedges' g) (Pegzilarginase – Placebo)	1.23	
			95% CI for SMD (Hedges' g)	-0.05, 2.52	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: N = Number of patients in the analysis; n = number of patients with event; SD = Standard deviation; SE = Standard error; LS = Least Squares; MMRM = Mixed Model Repeated Measures; CI = Confidence Interval; SMD = Standardized Mean Difference.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on an MMRM with visit, randomized study treatment, subgroup, interaction between subgroup and randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
[2] Based on an MMRM with visit, randomized study treatment, and interaction between visit and randomized study treatment as effects, and Baseline value included as a covariate. Default covariance structure type=unstructured.
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4.10.15.37 Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score responders ≥ 15 by gender

Gender	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	Interaction	Treatment*Gender, p-value Chi-Square[1]	0.9699	
Male	Week 12	n (%)	12 (100.00)	5 (71.43)
		Self-report: n (%)	7 (58.33)	1 (14.29)
		Parent Report: n (%)	4 (33.33)	3 (42.86)
		Number of patients with missing data: n (%)	0 (0.00)	2 (28.57)
		Number of patients imputed as non-responders: n (%)	1 (8.33)	1 (14.29)
		Non-Responders [1]	11 (91.67)	5 (100.00)
		Responders	1 (8.33)	0 (0.00)
		OR (95% CI)	1.43 (0.05, 41.23)	
		RR (95% CI)	1.38 (0.07, 29.26)	
		RD % (95% CI)	3.21 (-24.91, 31.32)	
		p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Table Generation: 11SEP2023 12:08:15 PM
Program: t-qs-categ-pedsql-sub.sas

Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score responders ≥ 15 by gender

Gender	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Male	Week 24	n (%)	12 (100.00)	5 (71.43)
		Self-report: n (%)	6 (50.00)	1 (14.29)
		Parent Report: n (%)	3 (25.00)	4 (57.14)
		Number of patients with missing data: n (%)	0 (0.00)	2 (28.57)
		Number of patients imputed as non-responders: n (%)	3 (25.00)	0 (0.00)
		Non-Responders [1]	11 (91.67)	4 (80.00)
		Responders	1 (8.33)	1 (20.00)
		OR (95% CI)	0.36 (0.02, 7.29)	
		RR (95% CI)	0.42 (0.03, 5.43)	
		RD % (95% CI)	-11.67 (-50.06, 26.72)	
		p-value – Fisher's Exact Test	0.5147	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score responders ≥ 15 by gender

Gender	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Week 12	n (%)	8 (88.89)	4 (100.00)
		Self-report: n (%)	3 (33.33)	3 (75.00)
		Parent Report: n (%)	5 (55.56)	0 (0.00)
		Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
		Number of patients imputed as non-responders: n (%)	0 (0.00)	1 (25.00)
		Non-Responders [1]	7 (87.50)	4 (100.00)
		Responders	1 (12.50)	0 (0.00)
		OR (95% CI)	1.80 (0.06, 54.33)	
		RR (95% CI)	1.67 (0.08, 33.75)	
		RD % (95% CI)	6.67 (-29.17, 42.50)	
		p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score responders ≥ 15 by gender

Gender	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Female	Week 24	n (%)	8 (88.89)	4 (100.00)
		Self-report: n (%)	3 (33.33)	3 (75.00)
		Parent Report: n (%)	5 (55.56)	0 (0.00)
		Number of patients with missing data: n (%)	1 (11.11)	0 (0.00)
		Number of patients imputed as non-responders: n (%)	0 (0.00)	1 (25.00)
		Non-Responders [1]	6 (75.00)	4 (100.00)
		Responders	2 (25.00)	0 (0.00)
		OR (95% CI)	3.46 (0.13, 90.68)	
		RR (95% CI)	2.78 (0.16, 47.20)	
		RD % (95% CI)	17.78 (-21.56, 57.12)	
		p-value – Fisher's Exact Test	0.5152	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
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4.10.15.38 Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score responders ≥ 15 by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	Interaction	Treatment*Age Group, p-value Chi-Square[1]	0.9553	
<10.5 years old at screening	Week 12	n (%)	12 (100.00)	4 (100.00)
		Self-report: n (%)	3 (25.00)	0 (0.00)
		Parent Report: n (%)	8 (66.67)	3 (75.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders: n (%)	1 (8.33)	1 (25.00)
		Non-Responders [1]	10 (83.33)	4 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	2.14 (0.08, 54.22)	
		RR (95% CI)	1.92 (0.11, 33.44)	
		RD % (95% CI)	9.23 (-24.69, 43.15)	
		p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score responders ≥ 15 by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
<10.5 years old at screening	Week 24	n (%)	12 (100.00)	4 (100.00)
		Self-report: n (%)	3 (25.00)	0 (0.00)
		Parent Report: n (%)	6 (50.00)	3 (75.00)
		Number of patients with missing data: n (%)	0 (0.00)	0 (0.00)
		Number of patients imputed as non-responders: n (%)	3 (25.00)	1 (25.00)
		Non-Responders [1]	9 (75.00)	4 (100.00)
		Responders	3 (25.00)	0 (0.00)
		OR (95% CI)	3.32 (0.14, 78.81)	
		RR (95% CI)	2.69 (0.17, 43.31)	
		RD % (95% CI)	16.92 (-18.75, 52.60)	
		p-value – Fisher's Exact Test	0.5286	
≥ 10.5 years old at screening	Week 12	n (%)	8 (88.89)	5 (71.43)
		Self-report: n (%)	7 (77.78)	4 (57.14)
		Parent Report: n (%)	1 (11.11)	0 (0.00)
		Number of patients with missing data: n (%)	1 (11.11)	2 (28.57)
		Number of patients imputed as non-responders: n (%)	0 (0.00)	1 (14.29)
		Non-Responders [1]	8 (100.00)	5 (100.00)

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
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Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score responders ≥ 15 by age group

Age Group	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ 10.5 years old at screening	Week 24	n (%)	8 (88.89)	5 (71.43)
		Self-report: n (%)	6 (66.67)	4 (57.14)
		Parent Report: n (%)	2 (22.22)	1 (14.29)
		Number of patients with missing data: n (%)	1 (11.11)	2 (28.57)
		Number of patients imputed as non-responders: n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	8 (100.00)	4 (80.00)
		Responders	0 (0.00)	1 (20.00)
		OR (95% CI)	0.18 (0.01, 5.28)	
		RR (95% CI)	0.22 (0.01, 4.60)	
		RD % (95% CI)	-19.44 (-57.19, 18.30)	
		p-value – Fisher's Exact Test	0.3846	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
Program: t-qs-categ-pedsql-sub.sas
Table Generation: 11SEP2023 12:08:22 PM

4.10.15.39 Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score responders ≥ 15 by region

Region	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	Interaction	Treatment*Region, p-value Chi-Square[1]	0.9699	
US	Week 12	n (%)	8 (100.00)	4 (66.67)
		Self-report: n (%)	4 (50.00)	1 (16.67)
		Parent Report: n (%)	4 (50.00)	3 (50.00)
		Number of patients with missing data: n (%)	0 (0.00)	2 (33.33)
		Number of patients imputed as non-responders: n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	8 (100.00)	4 (100.00)
	Week 24	n (%)	8 (100.00)	4 (66.67)
		Self-report: n (%)	4 (50.00)	1 (16.67)
		Parent Report: n (%)	4 (50.00)	3 (50.00)
		Number of patients with missing data: n (%)	0 (0.00)	2 (33.33)
		Number of patients imputed as non-responders: n (%)	0 (0.00)	0 (0.00)
		Non-Responders [1]	6 (75.00)	4 (100.00)
		Responders	2 (25.00)	0 (0.00)
		OR (95% CI)	3.46 (0.13, 90.68)	
		RR (95% CI)	2.78 (0.16, 47.20)	
		RD % (95% CI)	17.78 (-21.56, 57.12)	
		p-value – Fisher's Exact Test	0.5152	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Table Generation: 11SEP2023 12:08:29 PM
Program: t-qs-categ-pedsql-sub.sas

Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score responders ≥ 15 by region

Region	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Week 12	n (%)	12 (92.31)	5 (100.00)
		Self-report: n (%)	6 (46.15)	3 (60.00)
		Parent Report: n (%)	5 (38.46)	0 (0.00)
		Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
		Number of patients imputed as non-responders: n (%)	1 (7.69)	2 (40.00)
		Non-Responders [1]	10 (83.33)	5 (100.00)
		Responders	2 (16.67)	0 (0.00)
		OR (95% CI)	2.62 (0.11, 64.69)	
		RR (95% CI)	2.31 (0.13, 41.03)	
		RD % (95% CI)	10.90 (-19.89, 41.69)	
		p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Table Generation: 11SEP2023 12:08:29 PM
Program: t-qs-categ-pedsql-sub.sas

Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score responders ≥ 15 by region

Region	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
Non-US	Week 24	n (%)	12 (92.31)	5 (100.00)
		Self-report: n (%)	5 (38.46)	3 (60.00)
		Parent Report: n (%)	4 (30.77)	1 (20.00)
		Number of patients with missing data: n (%)	1 (7.69)	0 (0.00)
		Number of patients imputed as non-responders: n (%)	3 (23.08)	1 (20.00)
		Non-Responders [1]	11 (91.67)	4 (80.00)
		Responders	1 (8.33)	1 (20.00)
		OR (95% CI)	0.36 (0.02, 7.29)	
		RR (95% CI)	0.42 (0.03, 5.43)	
		RD % (95% CI)	-11.67 (-50.06, 26.72)	
		p-value – Fisher's Exact Test	0.5147	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Table Generation: 11SEP2023 12:08:29 PM
Program: t-qs-categ-pedsql-sub.sas

4.10.15.40 Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score responders ≥ 15 by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
All	Interaction	Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.9743	
I	Week 12	n (%)	9 (100.00)	4 (80.00)
		Self-report: n (%)	5 (55.56)	3 (60.00)
		Parent Report: n (%)	3 (33.33)	1 (20.00)
		Number of patients with missing data: n (%)	0 (0.00)	1 (20.00)
		Number of patients imputed as non-responders: n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	9 (100.00)	4 (100.00)
	Week 24	n (%)	9 (100.00)	4 (80.00)
		Self-report: n (%)	5 (55.56)	3 (60.00)
		Parent Report: n (%)	3 (33.33)	1 (20.00)
		Number of patients with missing data: n (%)	0 (0.00)	1 (20.00)
		Number of patients imputed as non-responders: n (%)	1 (11.11)	0 (0.00)
		Non-Responders [1]	8 (88.89)	4 (100.00)
		Responders	1 (11.11)	0 (0.00)
		OR (95% CI)	1.59 (0.05, 47.52)	
		RR (95% CI)	1.50 (0.07, 30.59)	
		RD % (95% CI)	5.00 (-29.37, 39.37)	
		p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Table Generation: 11SEP2023 12:08:35 PM
Program: t-qs-categ-pedsql-sub.sas

Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score responders ≥ 15 by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Week 12	n (%)	11 (91.67)	5 (83.33)
		Self-report: n (%)	5 (41.67)	1 (16.67)
		Parent Report: n (%)	6 (50.00)	2 (33.33)
		Number of patients with missing data: n (%)	1 (8.33)	1 (16.67)
		Number of patients imputed as non-responders: n (%)	0 (0.00)	2 (33.33)
		Non-Responders [1]	9 (81.82)	5 (100.00)
		Responders	2 (18.18)	0 (0.00)
		OR (95% CI)	2.89 (0.12, 71.93)	
		RR (95% CI)	2.50 (0.14, 44.26)	
		RD % (95% CI)	12.50 (-19.39, 44.39)	
		p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Table Generation: 11SEP2023 12:08:35 PM
Program: t-qs-categ-pedsql-sub.sas

Pediatric Quality of Life Inventory (PEDSQL) - Psychosocial Health Summary Score responders ≥ 15 by GMFCS

GMFCS at Baseline	Visit	Statistic	Pegzilarginase (N = 20) n (%)	Placebo (N = 9) n (%)
≥ II	Week 24	n (%)	11 (91.67)	5 (83.33)
		Self-report: n (%)	4 (33.33)	1 (16.67)
		Parent Report: n (%)	5 (41.67)	3 (50.00)
		Number of patients with missing data: n (%)	1 (8.33)	1 (16.67)
		Number of patients imputed as non-responders: n (%)	2 (16.67)	1 (16.67)
		Non-Responders [1]	9 (81.82)	4 (80.00)
		Responders	2 (18.18)	1 (20.00)
		OR (95% CI)	0.89 (0.06, 12.88)	
		RR (95% CI)	0.91 (0.11, 7.84)	
		RD % (95% CI)	-1.82 (-43.64, 40.00)	
		p-value – Fisher's Exact Test	1.0000	

NOTE: If available, self-report was used and if no self report was available parent report was used.
At Baseline 15 self-reports and 13 parent reports, at Week 12 14 self-reports and 12 parent reports, at Week 24 13 self-reports and 12 parent reports were used.
Abbreviations: CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD: Risk Difference; RR: Risk Ratio.
NOTE: PedsQL is only approved for patients aged 2-18 years. Patients outside this age range excluded.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
[2] Non-Responder-Imputation (NRI) of missing values.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Table Generation: 11SEP2023 12:08:35 PM
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4.10.16 Subgruppenanalysen für Verträglichkeitsendpunkte

4.10.16.1 Gesamtraten inklusive krankheitsbezogener Ereignisse

4.10.16.1.1 Patients with at least one TEAE by gender

Gender	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test: Treatment*Gender, p-value Chi-Square[1]	0.9971	
Male	Patients with any TEAEs	11 (91.67)	7 (100.00)
	Patients with no TEAEs	1 (8.33)	0 (0.00)
	OR (95% CI)	0.51 (0.02, 14.28)	
	RR (95% CI)	0.94 (0.72, 1.23)	
	RD % (95% CI)	-5.29 (-29.43, 18.86)	
	p-value – Fisher's Exact Test	1.0000	
Female	Patients with any TEAEs	7 (77.78)	4 (100.00)
	Patients with no TEAEs	2 (22.22)	0 (0.00)
	OR (95% CI)	0.33 (0.01, 8.63)	
	RR (95% CI)	0.83 (0.53, 1.32)	
	RD % (95% CI)	-15.00 (-52.57, 22.57)	
	p-value – Fisher's Exact Test	1.0000	

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
Program: t-teae-sub.sas
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4.10.16.1.2 Patients with at least one TEAE by age group

Age Group	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test: Treatment*Age Group, p-value Chi-Square[1]	0.9988	
<10.5 years old at screening	Patients with any TEAEs	10 (83.33)	4 (100.00)
	Patients with no TEAEs	2 (16.67)	0 (0.00)
	OR (95% CI)	0.47 (0.02, 11.81)	
	RR (95% CI)	0.90 (0.60, 1.33)	
	RD % (95% CI)	-9.23 (-43.15, 24.69)	
	p-value – Fisher's Exact Test	1.0000	
≥ 10.5 years old at screening	Patients with any TEAEs	8 (88.89)	7 (100.00)
	Patients with no TEAEs	1 (11.11)	0 (0.00)
	OR (95% CI)	0.38 (0.01, 10.74)	
	RR (95% CI)	0.91 (0.66, 1.24)	
	RD % (95% CI)	-8.75 (-36.52, 19.02)	
	p-value – Fisher's Exact Test	1.0000	

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
Program: t-teae-sub.sas
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4.10.16.1.3 Patients with at least one TEAE by region

Region	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test: Treatment*Region, p-value Chi-Square[1]	0.9994	
US	Patients with any TEAEs	7 (87.50)	6 (100.00)
	Patients with no TEAEs	1 (12.50)	0 (0.00)
	OR (95% CI)	0.38 (0.01, 11.17)	
	RR (95% CI)	0.90 (0.63, 1.28)	
	RD % (95% CI)	-9.52 (-40.46, 21.41)	
	p-value – Fisher's Exact Test	1.0000	
Non-US	Patients with any TEAEs	11 (84.62)	5 (100.00)
	Patients with no TEAEs	2 (15.38)	0 (0.00)
	OR (95% CI)	0.42 (0.02, 10.28)	
	RR (95% CI)	0.90 (0.64, 1.26)	
	RD % (95% CI)	-9.52 (-39.38, 20.34)	
	p-value – Fisher's Exact Test	1.0000	

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
Program: t-teae-sub.sas
Table Generation: 11SEP2023 3:07:32 PM

4.10.16.1.4 Patients with at least one TEAE by GMFCS level at baseline

GMFCS at Baseline	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test: Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.9738	
I	Patients with any TEAEs	9 (100.00)	5 (100.00)
	Patients with no TEAEs	0 (0.00)	0 (0.00)
≥ II	Patients with any TEAEs	9 (75.00)	6 (100.00)
	Patients with no TEAEs	3 (25.00)	0 (0.00)
	OR (95% CI)	0.21 (0.01, 4.76)	
	RR (95% CI)	0.79 (0.53, 1.16)	
	RD % (95% CI)	-19.78 (-50.53, 10.97)	
	p-value – Fisher's Exact Test	0.5147	

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
Program: t-teae-sub.sas
Table Generation: 11SEP2023 3:07:38 PM

4.10.16.1.5 Patients with at least one mild TEAE by gender

Gender	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test: Treatment*Gender, p-value Chi-Square[1]	0.9718	
Male	Patients with any mild TEAEs	10 (83.33)	6 (85.71)
	Patients with no mild TEAEs	2 (16.67)	1 (14.29)
	OR (95% CI)	0.83 (0.06, 11.28)	
	RR (95% CI)	0.97 (0.66, 1.44)	
	RD % (95% CI)	-2.38 (-35.80, 31.03)	
	p-value – Fisher's Exact Test	1.0000	
Female	Patients with any mild TEAEs	7 (77.78)	4 (100.00)
	Patients with no mild TEAEs	2 (22.22)	0 (0.00)
	OR (95% CI)	0.33 (0.01, 8.63)	
	RR (95% CI)	0.83 (0.53, 1.32)	
	RD % (95% CI)	-15.00 (-52.57, 22.57)	
	p-value – Fisher's Exact Test	1.0000	

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
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Table Generation: 11SEP2023 3:07:46 PM

4.10.16.1.6 Patients with at least one mild TEAE by age group

Age Group	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test: Treatment*Age Group, p-value Chi-Square[1]	0.9740	
<10.5 years old at screening	Patients with any mild TEAEs	10 (83.33)	3 (75.00)
	Patients with no mild TEAEs	2 (16.67)	1 (25.00)
	OR (95% CI)	1.67 (0.11, 25.43)	
	RR (95% CI)	1.11 (0.60, 2.07)	
	RD % (95% CI)	8.33 (-39.05, 55.72)	
	p-value – Fisher's Exact Test	1.0000	
≥ 10.5 years old at screening	Patients with any mild TEAEs	7 (77.78)	7 (100.00)
	Patients with no mild TEAEs	2 (22.22)	0 (0.00)
	OR (95% CI)	0.20 (0.01, 4.91)	
	RR (95% CI)	0.80 (0.54, 1.19)	
	RD % (95% CI)	-18.75 (-50.40, 12.90)	
	p-value – Fisher's Exact Test	0.4750	

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
NOTE: Median age used as cut-off point.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
Program: t-teae-sub.sas
Table Generation: 11SEP2023 3:07:52 PM

4.10.16.1.7 Patients with at least one mild TEAE by region

Region	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test: Treatment*Region, p-value Chi-Square[1]	0.9669	
US	Patients with any mild TEAEs	7 (87.50)	5 (83.33)
	Patients with no mild TEAEs	1 (12.50)	1 (16.67)
	OR (95% CI)	1.40 (0.07, 28.12)	
	RR (95% CI)	1.05 (0.67, 1.64)	
	RD % (95% CI)	4.17 (-33.44, 41.78)	
	p-value – Fisher's Exact Test	1.0000	
Non-US	Patients with any mild TEAEs	10 (76.92)	5 (100.00)
	Patients with no mild TEAEs	3 (23.08)	0 (0.00)
	OR (95% CI)	0.27 (0.01, 6.29)	
	RR (95% CI)	0.82 (0.56, 1.20)	
	RD % (95% CI)	-16.67 (-48.35, 15.01)	
	p-value – Fisher's Exact Test	0.5221	

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
Program: t-teae-sub.sas
Table Generation: 11SEP2023 3:07:59 PM

4.10.16.1.8 Patients with at least one mild TEAE by GMFCS level at baseline

GMFCS at Baseline	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test: Treatment*GMFCS at Baseline, p-value Chi-Square[1]	0.9716	
I	Patients with any mild TEAEs	8 (88.89)	5 (100.00)
	Patients with no mild TEAEs	1 (11.11)	0 (0.00)
	OR (95% CI)	0.52 (0.02, 15.06)	
	RR (95% CI)	0.93 (0.65, 1.32)	
	RD % (95% CI)	-6.67 (-37.95, 24.62)	
	p-value – Fisher's Exact Test	1.0000	
≥ II	Patients with any mild TEAEs	9 (75.00)	5 (83.33)
	Patients with no mild TEAEs	3 (25.00)	1 (16.67)
	OR (95% CI)	0.60 (0.05, 7.41)	
	RR (95% CI)	0.90 (0.55, 1.46)	
	RD % (95% CI)	-8.33 (-46.93, 30.26)	
	p-value – Fisher's Exact Test	1.0000	

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
Program: t-teae-sub.sas
Table Generation: 11SEP2023 3:08:06 PM

4.10.16.1.9 Patients with at least one moderate TEAE by gender

Gender	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Patients with any moderate TEAEs	5 (41.67)	3 (42.86)
	Patients with no moderate TEAEs	7 (58.33)	4 (57.14)
	Threshold for subgroup analysis not reached		
Female	Patients with any moderate TEAEs	3 (33.33)	3 (75.00)
	Patients with no moderate TEAEs	6 (66.67)	1 (25.00)
	Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Program: t-teae-sub2.sas
Table Generation: 11SEP2023 2:59:04 PM

4.10.16.1.10 Patients with at least one moderate TEAE by age group

Age Group	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Patients with any moderate TEAEs	3 (25.00)	2 (50.00)
	Patients with no moderate TEAEs	9 (75.00)	2 (50.00)
	Threshold for subgroup analysis not reached		
≥ 10.5 years old at screening	Patients with any moderate TEAEs	5 (55.56)	4 (57.14)
	Patients with no moderate TEAEs	4 (44.44)	3 (42.86)
	Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
Program: t-teae-sub2.sas
Table Generation: 11SEP2023 2:59:26 PM

4.10.16.1.11 Patients with at least one moderate TEAE by region

Region	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
All	Interaction test: Treatment*Region, p-value Chi-Square[1]	0.3240	
US	Patients with any moderate TEAEs	1 (12.50)	3 (50.00)
	Patients with no moderate TEAEs	7 (87.50)	3 (50.00)
	OR (95% CI)	0.14 (0.01, 1.99)	
	RR (95% CI)	0.25 (0.03, 1.85)	
	RD % (95% CI)	-37.50 (-83.61, 8.61)	
	p-value – Fisher's Exact Test	0.2448	
Non-US	Patients with any moderate TEAEs	7 (53.85)	3 (60.00)
	Patients with no moderate TEAEs	6 (46.15)	2 (40.00)
	OR (95% CI)	0.78 (0.10, 6.32)	
	RR (95% CI)	0.90 (0.37, 2.15)	
	RD % (95% CI)	-6.15 (-56.93, 44.62)	
	p-value – Fisher's Exact Test	1.0000	

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
[1] Based on logistic model with randomized study treatment, subgroup, and interaction between subgroup and randomized study treatment as effects.
Program: t-teae-sub.sas
Table Generation: 11SEP2023 3:08:12 PM

4.10.16.1.12 Patients with at least one moderate TEAE by GMFCS level at baseline

GMFCS at Baseline	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Patients with any moderate TEAEs	3 (33.33)	3 (60.00)
	Patients with no moderate TEAEs	6 (66.67)	2 (40.00)
	Threshold for subgroup analysis not reached		
≥ II	Patients with any moderate TEAEs	5 (41.67)	3 (50.00)
	Patients with no moderate TEAEs	7 (58.33)	3 (50.00)
	Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Program: t-teae-sub2.sas
Table Generation: 11SEP2023 2:59:34 PM

4.10.16.1.13 Patients with at least one severe TEAE by gender

Gender	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Patients with any severe TEAEs	0 (0.00)	0 (0.00)
	Patients with no severe TEAEs	12 (100.00)	7 (100.00)
	Threshold for subgroup analysis not reached		
Female	Patients with any severe TEAEs	1 (11.11)	0 (0.00)
	Patients with no severe TEAEs	8 (88.89)	4 (100.00)
	Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Program: t-teae-sub2.sas
Table Generation: 11SEP2023 2:59:43 PM

4.10.16.1.14 Patients with at least one severe TEAE by age group

Age Group	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Patients with any severe TEAEs	0 (0.00)	0 (0.00)
	Patients with no severe TEAEs	12 (100.00)	4 (100.00)
	Threshold for subgroup analysis not reached		
≥ 10.5 years old at screening	Patients with any severe TEAEs	1 (11.11)	0 (0.00)
	Patients with no severe TEAEs	8 (88.89)	7 (100.00)
	Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
Program: t-teae-sub2.sas
Table Generation: 11SEP2023 2:59:50 PM

4.10.16.1.15 Patients with at least one severe TEAE by region

Region	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Patients with any severe TEAEs	0 (0.00)	0 (0.00)
	Patients with no severe TEAEs	8 (100.00)	6 (100.00)
	Threshold for subgroup analysis not reached		
Non-US	Patients with any severe TEAEs	1 (7.69)	0 (0.00)
	Patients with no severe TEAEs	12 (92.31)	5 (100.00)
	Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Program: t-teae-sub2.sas
Table Generation: 11SEP2023 2:59:57 PM

4.10.16.1.16 Patients with at least one severe TEAE by GMFCS level at baseline

GMFCS at Baseline	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Patients with any severe TEAEs	1 (11.11)	0 (0.00)
	Patients with no severe TEAEs	8 (88.89)	5 (100.00)
	Threshold for subgroup analysis not reached		
≥ II	Patients with any severe TEAEs	0 (0.00)	0 (0.00)
	Patients with no severe TEAEs	12 (100.00)	6 (100.00)
	Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Program: t-teae-sub2.sas
Table Generation: 11SEP2023 3:00:04 PM

4.10.16.1.17 Patients with at least one treatment emergent SAE by gender

Gender	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Patients with any treatment emergent SAE	2 (16.67)	2 (28.57)
	Patients with no treatment emergent SAE	10 (83.33)	5 (71.43)
	Threshold for subgroup analysis not reached		
Female	Patients with any treatment emergent SAE	2 (22.22)	2 (50.00)
	Patients with no treatment emergent SAE	7 (77.78)	2 (50.00)
	Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Program: t-teae-sub2.sas
Table Generation: 11SEP2023 3:00:11 PM

4.10.16.1.18 Patients with at least one treatment emergent SAE by age group

Age Group	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Patients with any treatment emergent SAE	1 (8.33)	2 (50.00)
	Patients with no treatment emergent SAE	11 (91.67)	2 (50.00)
	Threshold for subgroup analysis not reached		
≥ 10.5 years old at screening	Patients with any treatment emergent SAE	3 (33.33)	2 (28.57)
	Patients with no treatment emergent SAE	6 (66.67)	5 (71.43)
	Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
Program: t-teae-sub2.sas
Table Generation: 11SEP2023 3:00:18 PM

4.10.16.1.19 Patients with at least one treatment emergent SAE by region

Region	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Patients with any treatment emergent SAE	1 (12.50)	2 (33.33)
	Patients with no treatment emergent SAE	7 (87.50)	4 (66.67)
	Threshold for subgroup analysis not reached		
Non-US	Patients with any treatment emergent SAE	3 (23.08)	2 (40.00)
	Patients with no treatment emergent SAE	10 (76.92)	3 (60.00)
	Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Program: t-teae-sub2.sas
Table Generation: 11SEP2023 3:00:24 PM

4.10.16.1.20 Patients with at least one treatment emergent SAE by GMFCS level at baseline

GMFCS at Baseline	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Patients with any treatment emergent SAE	1 (11.11)	2 (40.00)
	Patients with no treatment emergent SAE	8 (88.89)	3 (60.00)
	Threshold for subgroup analysis not reached		
≥ II	Patients with any treatment emergent SAE	3 (25.00)	2 (33.33)
	Patients with no treatment emergent SAE	9 (75.00)	4 (66.67)
	Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Program: t-teae-sub2.sas
Table Generation: 11SEP2023 3:00:32 PM

4.10.16.1.21 Patients with at least one hypersensitivity reaction (independent of severity) by gender

Gender	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Patients with any hypersensitivity reactions	1 (8.33)	0 (0.00)
	Patients with no hypersensitivity reactions	11 (91.67)	7 (100.00)
	Threshold for subgroup analysis not reached [1]		
Female	Patients with any hypersensitivity reactions	1 (11.11)	0 (0.00)
	Patients with no hypersensitivity reactions	8 (88.89)	4 (100.00)
	Threshold for subgroup analysis not reached [1]		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
[1] Threshold for subgroup analysis independent of severity not reached thus subgroup analysis by severity not performed either.
Program: t-teae-sub2.sas
Table Generation: 11SEP2023 3:00:38 PM

4.10.16.1.22 Patients with at least one hypersensitivity reaction (independent of severity) by age group

Age Group	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Patients with any hypersensitivity reactions	1 (8.33)	0 (0.00)
	Patients with no hypersensitivity reactions	11 (91.67)	4 (100.00)
	Threshold for subgroup analysis not reached [1]		
≥ 10.5 years old at screening	Patients with any hypersensitivity reactions	1 (11.11)	0 (0.00)
	Patients with no hypersensitivity reactions	8 (88.89)	7 (100.00)
	Threshold for subgroup analysis not reached [1]		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
[1] Threshold for subgroup analysis independent of severity not reached thus subgroup analysis by severity not performed either.
NOTE: Median age used as cut-off point.
Program: t-teae-sub2.sas
Table Generation: 11SEP2023 3:00:46 PM

4.10.16.1.23 Patients with at least one hypersensitivity reaction (independent of severity) by region

Region	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Patients with any hypersensitivity reactions	0 (0.00)	0 (0.00)
	Patients with no hypersensitivity reactions	8 (100.00)	6 (100.00)
	Threshold for subgroup analysis not reached [1]		
Non-US	Patients with any hypersensitivity reactions	2 (15.38)	0 (0.00)
	Patients with no hypersensitivity reactions	11 (84.62)	5 (100.00)
	Threshold for subgroup analysis not reached [1]		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
[1] Threshold for subgroup analysis independent of severity not reached thus subgroup analysis by severity not performed either.
Program: t-teae-sub2.sas
Table Generation: 11SEP2023 3:00:53 PM

4.10.16.1.24 Patients with at least one hypersensitivity reaction (independent of severity) by GMFCS level at baseline

GMFCS at Baseline	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Patients with any hypersensitivity reactions	1 (11.11)	0 (0.00)
	Patients with no hypersensitivity reactions	8 (88.89)	5 (100.00)
	Threshold for subgroup analysis not reached [1]		
≥ II	Patients with any hypersensitivity reactions	1 (8.33)	0 (0.00)
	Patients with no hypersensitivity reactions	11 (91.67)	6 (100.00)
	Threshold for subgroup analysis not reached [1]		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
[1] Threshold for subgroup analysis independent of severity not reached thus subgroup analysis by severity not performed either.
Program: t-teae-sub2.sas
Table Generation: 11SEP2023 3:01:01 PM

4.10.16.1.25 Patients with at least one hyperammonemic episode (independent of severity) by gender

Gender	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Patients with any hyperammonemic episodes	1 (8.33)	2 (28.57)
	Patients with no hyperammonemic episodes	11 (91.67)	5 (71.43)
	Threshold for subgroup analysis not reached [1]		
Female	Patients with any hyperammonemic episodes	2 (22.22)	2 (50.00)
	Patients with no hyperammonemic episodes	7 (77.78)	2 (50.00)
	Threshold for subgroup analysis not reached [1]		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
[1] Threshold for subgroup analysis independent of severity not reached thus subgroup analysis by severity not performed either.
Program: t-teae-sub2.sas
Table Generation: 11SEP2023 3:01:08 PM

4.10.16.1.26 Patients with at least one hyperammonemic episode (independent of severity) by age group

Age Group	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Patients with any hyperammonemic episodes	0 (0.00)	2 (50.00)
	Patients with no hyperammonemic episodes	12 (100.00)	2 (50.00)
	Threshold for subgroup analysis not reached [1]		
≥ 10.5 years old at screening	Patients with any hyperammonemic episodes	3 (33.33)	2 (28.57)
	Patients with no hyperammonemic episodes	6 (66.67)	5 (71.43)
	Threshold for subgroup analysis not reached [1]		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
[1] Threshold for subgroup analysis independent of severity not reached thus subgroup analysis by severity not performed either.
NOTE: Median age used as cut-off point.
Program: t-teae-sub2.sas
Table Generation: 11SEP2023 3:01:15 PM

4.10.16.1.27 Patients with at least one hyperammonemic episode (independent of severity) by region

Region	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Patients with any hyperammonemic episodes	1 (12.50)	2 (33.33)
	Patients with no hyperammonemic episodes	7 (87.50)	4 (66.67)
	Threshold for subgroup analysis not reached [1]		
Non-US	Patients with any hyperammonemic episodes	2 (15.38)	2 (40.00)
	Patients with no hyperammonemic episodes	11 (84.62)	3 (60.00)
	Threshold for subgroup analysis not reached [1]		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
[1] Threshold for subgroup analysis independent of severity not reached thus subgroup analysis by severity not performed either.
Program: t-teae-sub2.sas
Table Generation: 11SEP2023 3:01:22 PM

4.10.16.1.28 Patients with at least one hyperammonemic episode (independent of severity) by GMFCS level at baseline

GMFCS at Baseline	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Patients with any hyperammonemic episodes	1 (11.11)	2 (40.00)
	Patients with no hyperammonemic episodes	8 (88.89)	3 (60.00)
	Threshold for subgroup analysis not reached [1]		
≥ II	Patients with any hyperammonemic episodes	2 (16.67)	2 (33.33)
	Patients with no hyperammonemic episodes	10 (83.33)	4 (66.67)
	Threshold for subgroup analysis not reached [1]		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
[1] Threshold for subgroup analysis independent of severity not reached thus subgroup analysis by severity not performed either.
Program: t-teae-sub2.sas
Table Generation: 11SEP2023 3:01:28 PM

4.10.16.1.29 Any liver function Test TEAE (independent of severity) by gender

Gender	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Patients with any liver function test TEAEs	1 (8.33)	2 (28.57)
	Patients with no liver function test TEAEs	11 (91.67)	5 (71.43)
	Threshold for subgroup analysis not reached [1]		
Female	Patients with any liver function test TEAEs	3 (33.33)	0 (0.00)
	Patients with no liver function test TEAEs	6 (66.67)	4 (100.00)
	Threshold for subgroup analysis not reached [1]		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
[1] Threshold for subgroup analysis independent of severity not reached thus subgroup analysis by severity not performed either.
Program: t-teae-sub2.sas
Table Generation: 11SEP2023 3:01:35 PM

4.10.16.1.30 Any liver function Test TEAE (independent of severity) by age group

Age Group	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Patients with any liver function test TEAEs	1 (8.33)	1 (25.00)
	Patients with no liver function test TEAEs	11 (91.67)	3 (75.00)
	Threshold for subgroup analysis not reached [1]		
≥ 10.5 years old at screening	Patients with any liver function test TEAEs	3 (33.33)	1 (14.29)
	Patients with no liver function test TEAEs	6 (66.67)	6 (85.71)
	Threshold for subgroup analysis not reached [1]		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
[1] Threshold for subgroup analysis independent of severity not reached thus subgroup analysis by severity not performed either.
NOTE: Median age used as cut-off point.
Program: t-teae-sub2.sas
Table Generation: 11SEP2023 3:01:42 PM

4.10.16.1.31 Any liver function Test TEAE (independent of severity) by region

Region	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Patients with any liver function test TEAEs	0 (0.00)	1 (16.67)
	Patients with no liver function test TEAEs	8 (100.00)	5 (83.33)
	Threshold for subgroup analysis not reached [1]		
Non-US	Patients with any liver function test TEAEs	4 (30.77)	1 (20.00)
	Patients with no liver function test TEAEs	9 (69.23)	4 (80.00)
	Threshold for subgroup analysis not reached [1]		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
[1] Threshold for subgroup analysis independent of severity not reached thus subgroup analysis by severity not performed either.
Program: t-teae-sub2.sas
Table Generation: 11SEP2023 3:01:50 PM

4.10.16.1.32 Any liver function Test TEAE (independent of severity) by GMFCS level at baseline

GMFCS at Baseline	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Patients with any liver function test TEAEs	1 (11.11)	0 (0.00)
	Patients with no liver function test TEAEs	8 (88.89)	5 (100.00)
	Threshold for subgroup analysis not reached [1]		
≥ II	Patients with any liver function test TEAEs	3 (25.00)	2 (33.33)
	Patients with no liver function test TEAEs	9 (75.00)	4 (66.67)
	Threshold for subgroup analysis not reached [1]		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
[1] Threshold for subgroup analysis independent of severity not reached thus subgroup analysis by severity not performed either.
Program: t-teae-sub2.sas
Table Generation: 11SEP2023 3:01:57 PM

4.10.16.1.33 Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Blood and lymphatic system disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Anaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Eye disorders	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Eyelid oedema	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Eye disorders	Ocular hyperaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Gastrointestinal disorders	Total	Patients with any TEAEs	7 (33.33)	4 (36.36)
			Patients with no TEAEs	14 (66.67)	7 (63.64)
			OR (95% CI)	0.88 (0.19, 4.03)	
			RR (95% CI)	0.92 (0.34, 2.46)	
			RD % (95% CI)	-3.03 (-37.88, 31.82)	
			p-value – Fisher's Exact Test	1.0000	
		Abdominal discomfort	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Gastrointestinal disorders	Abdominal pain	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Constipation	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Diarrhoea	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Haematochezia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Gastrointestinal disorders	Nausea	Patients with any TEAEs	0 (0.00)	3 (27.27)
			Patients with no TEAEs	21 (100.00)	8 (72.73)
			Threshold for subgroup analysis not reached		
		Oral pain	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Vomiting	Patients with any TEAEs	4 (19.05)	3 (27.27)
			Patients with no TEAEs	17 (80.95)	8 (72.73)
			Threshold for subgroup analysis not reached		
	General disorders and administration site conditions	Total	Patients with any TEAEs	3 (14.29)	0 (0.00)
			Patients with no TEAEs	18 (85.71)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	General disorders and administration site conditions	Pyrexia	Patients with any TEAEs	3 (14.29)	0 (0.00)
			Patients with no TEAEs	18 (85.71)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Immune system disorders	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Food allergy	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Hypersensitivity	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Infections and infestations	Total	Patients with any TEAEs	5 (23.81)	0 (0.00)
			Patients with no TEAEs	16 (76.19)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Conjunctivitis	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Fungal skin infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Influenza	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Infections and infestations	Nasopharyngitis	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Pharyngitis	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Upper respiratory tract infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Injury, poisoning and procedural complications	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Injury, poisoning and procedural complications	Contusion	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Eye injury	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Fall	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Investigations	Total	Patients with any TEAEs	3 (14.29)	2 (18.18)
			Patients with no TEAEs	18 (85.71)	9 (81.82)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Investigations	Ammonia increased	Patients with any TEAEs	1 (4.76)	2 (18.18)
			Patients with no TEAEs	20 (95.24)	9 (81.82)
			Threshold for subgroup analysis not reached		
		Blood pressure increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Body temperature increased	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Cardiac murmur	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Metabolism and nutrition disorders	Total	Patients with any TEAEs	1 (4.76)	3 (27.27)
			Patients with no TEAEs	20 (95.24)	8 (72.73)
			Threshold for subgroup analysis not reached		
		Decreased appetite	Patients with any TEAEs	0 (0.00)	2 (18.18)
			Patients with no TEAEs	21 (100.00)	9 (81.82)
			Threshold for subgroup analysis not reached		
		Hyperammonaemia	Patients with any TEAEs	1 (4.76)	2 (18.18)
			Patients with no TEAEs	20 (95.24)	9 (81.82)
			Threshold for subgroup analysis not reached		
	Musculoskeletal and connective tissue disorders	Total	Patients with any TEAEs	1 (4.76)	2 (18.18)
			Patients with no TEAEs	20 (95.24)	9 (81.82)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Musculoskeletal and connective tissue disorders	Arthralgia	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Muscle spasms	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Osteochondrosis	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Pain in extremity	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Nervous system disorders	Total	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Headache	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Lethargy	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Psychiatric disorders	Total	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Psychiatric disorders	Mood altered	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Respiratory, thoracic and mediastinal disorders	Total	Patients with any TEAEs	3 (14.29)	1 (9.09)
			Patients with no TEAEs	18 (85.71)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Cough	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Nasal congestion	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Respiratory, thoracic and mediastinal disorders	Nasal inflammation	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Oropharyngeal pain	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Skin and subcutaneous tissue disorders	Total	Patients with any TEAEs	2 (9.52)	2 (18.18)
			Patients with no TEAEs	19 (90.48)	9 (81.82)
			Threshold for subgroup analysis not reached		
		Dry skin	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Skin and subcutaneous tissue disorders	Rash	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Skin exfoliation	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Vascular disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Hypertension	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Blood and lymphatic system disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Iron deficiency anaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Eye disorders	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Eye irritation	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Eye disorders	Eye pain	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Gastrointestinal disorders	Total	Patients with any TEAEs	3 (14.29)	2 (18.18)
			Patients with no TEAEs	18 (85.71)	9 (81.82)
			OR (95% CI)	0.75 (0.11, 5.32)	
			RR (95% CI)	0.79 (0.15, 4.03)	
			RD % (95% CI)	-3.90 (-31.16, 23.37)	
			p-value – Fisher's Exact Test	1.0000	
		Abdominal pain	Patients with any TEAEs	0 (0.00)	2 (18.18)
			Patients with no TEAEs	21 (100.00)	9 (81.82)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Gastrointestinal disorders	Abdominal pain upper	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Anal rash	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Constipation	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Diarrhoea	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Gastrointestinal disorders	Nausea	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Vomiting	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
	General disorders and administration site conditions	Total	Patients with any TEAEs	4 (19.05)	0 (0.00)
			Patients with no TEAEs	17 (80.95)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Administration site extravasation	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	General disorders and administration site conditions	Asthenia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Illness	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Infusion site extravasation	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Oedema peripheral	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	General disorders and administration site conditions	Peripheral swelling	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Pyrexia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Swelling face	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Hepatobiliary disorders	Total	Patients with any TEAEs	2 (9.52)	1 (9.09)
			Patients with no TEAEs	19 (90.48)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Hepatobiliary disorders	Cholelithiasis	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Hepatic cytolysis	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Infections and infestations	Total	Patients with any TEAEs	3 (14.29)	0 (0.00)
			Patients with no TEAEs	18 (85.71)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Gastrointestinal viral infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Infections and infestations	Nasopharyngitis	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Respiratory syncytial virus infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Viral infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Injury, poisoning and procedural complications	Total	Patients with any TEAEs	3 (14.29)	0 (0.00)
			Patients with no TEAEs	18 (85.71)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Injury, poisoning and procedural complications	Fall	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Procedural pain	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Scratch	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Investigations	Total	Patients with any TEAEs	4 (19.05)	1 (9.09)
			Patients with no TEAEs	17 (80.95)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Investigations	Activated partial thromboplastin time prolonged	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Alanine aminotransferase increased	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Amino acid level increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Ammonia increased	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Investigations	Aspartate aminotransferase increased	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Blood alkaline phosphatase increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Blood potassium decreased	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Cardiac murmur	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Investigations	Electroencephalogram abnormal	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		International normalised ratio increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Prothrombin time prolonged	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Metabolism and nutrition disorders	Total	Patients with any TEAEs	2 (9.52)	1 (9.09)
			Patients with no TEAEs	19 (90.48)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Metabolism and nutrition disorders	Hyperammonaemia	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Hypokalaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Vitamin D deficiency	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Vitamin K deficiency	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Metabolism and nutrition disorders	Zinc deficiency	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Nervous system disorders	Total	Patients with any TEAEs	4 (19.05)	2 (18.18)
			Patients with no TEAEs	17 (80.95)	9 (81.82)
			Threshold for subgroup analysis not reached		
		Disturbance in attention	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Dizziness	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Nervous system disorders	Headache	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Hyperammonaemic encephalopathy	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Lethargy	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Seizure	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Nervous system disorders	Tonic convulsion	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Psychiatric disorders	Total	Patients with any TEAEs	2 (9.52)	1 (9.09)
			Patients with no TEAEs	19 (90.48)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Behaviour disorder	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Generalised anxiety disorder	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Psychiatric disorders	Panic attack	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Respiratory, thoracic and mediastinal disorders	Total	Patients with any TEAEs	2 (9.52)	1 (9.09)
			Patients with no TEAEs	19 (90.48)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Cough	Patients with any TEAEs	2 (9.52)	1 (9.09)
			Patients with no TEAEs	19 (90.48)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Rhinorrhoea	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Skin and subcutaneous tissue disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Pruritus	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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4.10.16.1.34 Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Eye disorders	Total	Patients with any TEAEs	3 (14.29)	0 (0.00)
			Patients with no TEAEs	18 (85.71)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Eye pain	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Eyelid oedema	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Ocular hyperaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Gastrointestinal disorders	Total	Patients with any TEAEs	6 (28.57)	1 (9.09)
			Patients with no TEAEs	15 (71.43)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Abdominal pain	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Anal rash	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Constipation	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Gastrointestinal disorders	Haematochezia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Nausea	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Oral pain	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Vomiting	Patients with any TEAEs	2 (9.52)	1 (9.09)
			Patients with no TEAEs	19 (90.48)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	General disorders and administration site conditions	Total	Patients with any TEAEs	4 (19.05)	0 (0.00)
			Patients with no TEAEs	17 (80.95)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Illness	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Peripheral swelling	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Pyrexia	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Immune system disorders	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Food allergy	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Hypersensitivity	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Infections and infestations	Total	Patients with any TEAEs	7 (33.33)	0 (0.00)
			Patients with no TEAEs	14 (66.67)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Infections and infestations	Conjunctivitis	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Fungal skin infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Gastrointestinal viral infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Influenza	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Infections and infestations	Nasopharyngitis	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Pharyngitis	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Respiratory syncytial virus infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Viral infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Injury, poisoning and procedural complications	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Eye injury	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Procedural pain	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Investigations	Total	Patients with any TEAEs	3 (14.29)	1 (9.09)
			Patients with no TEAEs	18 (85.71)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Investigations	Ammonia increased	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Blood pressure increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Body temperature increased	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Electroencephalogram abnormal	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Metabolism and nutrition disorders	Total	Patients with any TEAEs	0 (0.00)	2 (18.18)
			Patients with no TEAEs	21 (100.00)	9 (81.82)
			Threshold for subgroup analysis not reached		
		Decreased appetite	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Hyperammonaemia	Patients with any TEAEs	0 (0.00)	2 (18.18)
			Patients with no TEAEs	21 (100.00)	9 (81.82)
			Threshold for subgroup analysis not reached		
	Musculoskeletal and connective tissue disorders	Total	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Musculoskeletal and connective tissue disorders	Muscle spasms	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Pain in extremity	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Nervous system disorders	Total	Patients with any TEAEs	2 (9.52)	1 (9.09)
			Patients with no TEAEs	19 (90.48)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Dizziness	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Nervous system disorders	Headache	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Lethargy	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Psychiatric disorders	Total	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Mood altered	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Respiratory, thoracic and mediastinal disorders	Total	Patients with any TEAEs	4 (19.05)	1 (9.09)
			Patients with no TEAEs	17 (80.95)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Cough	Patients with any TEAEs	4 (19.05)	1 (9.09)
			Patients with no TEAEs	17 (80.95)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Nasal congestion	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Nasal inflammation	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Respiratory, thoracic and mediastinal disorders	Rhinorrhoea	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Skin and subcutaneous tissue disorders	Total	Patients with any TEAEs	1 (4.76)	2 (18.18)
			Patients with no TEAEs	20 (95.24)	9 (81.82)
			Threshold for subgroup analysis not reached		
		Rash	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Skin exfoliation	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Vascular disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Hypertension	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
≥ 10.5 years old at screening	Blood and lymphatic system disorders	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Anaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Blood and lymphatic system disorders	Iron deficiency anaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Eye disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Eye irritation	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Gastrointestinal disorders	Total	Patients with any TEAEs	4 (19.05)	5 (45.45)
			Patients with no TEAEs	17 (80.95)	6 (54.55)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Gastrointestinal disorders	Abdominal discomfort	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Abdominal pain	Patients with any TEAEs	0 (0.00)	2 (18.18)
			Patients with no TEAEs	21 (100.00)	9 (81.82)
			Threshold for subgroup analysis not reached		
		Abdominal pain upper	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Constipation	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Gastrointestinal disorders	Diarrhoea	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Nausea	Patients with any TEAEs	1 (4.76)	3 (27.27)
			Patients with no TEAEs	20 (95.24)	8 (72.73)
			Threshold for subgroup analysis not reached		
		Vomiting	Patients with any TEAEs	4 (19.05)	2 (18.18)
			Patients with no TEAEs	17 (80.95)	9 (81.82)
			Threshold for subgroup analysis not reached		
	General disorders and administration site conditions	Total	Patients with any TEAEs	3 (14.29)	0 (0.00)
			Patients with no TEAEs	18 (85.71)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	General disorders and administration site conditions	Administration site extravasation	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Asthenia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Infusion site extravasation	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Oedema peripheral	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	General disorders and administration site conditions	Pyrexia	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Swelling face	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Hepatobiliary disorders	Total	Patients with any TEAEs	2 (9.52)	1 (9.09)
			Patients with no TEAEs	19 (90.48)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Cholelithiasis	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Hepatobiliary disorders	Hepatic cytolysis	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Infections and infestations	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Upper respiratory tract infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Injury, poisoning and procedural complications	Total	Patients with any TEAEs	3 (14.29)	0 (0.00)
			Patients with no TEAEs	18 (85.71)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Injury, poisoning and procedural complications	Contusion	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Fall	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Scratch	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Investigations	Total	Patients with any TEAEs	4 (19.05)	2 (18.18)
			Patients with no TEAEs	17 (80.95)	9 (81.82)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Investigations	Activated partial thromboplastin time prolonged	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Alanine aminotransferase increased	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Amino acid level increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Ammonia increased	Patients with any TEAEs	2 (9.52)	1 (9.09)
			Patients with no TEAEs	19 (90.48)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Investigations	Aspartate aminotransferase increased	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Blood alkaline phosphatase increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Blood potassium decreased	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Cardiac murmur	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Investigations	International normalised ratio increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Prothrombin time prolonged	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Metabolism and nutrition disorders	Total	Patients with any TEAEs	3 (14.29)	2 (18.18)
			Patients with no TEAEs	18 (85.71)	9 (81.82)
			Threshold for subgroup analysis not reached		
		Decreased appetite	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Metabolism and nutrition disorders	Hyperammonaemia	Patients with any TEAEs	2 (9.52)	1 (9.09)
			Patients with no TEAEs	19 (90.48)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Hypokalaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Vitamin D deficiency	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Vitamin K deficiency	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Metabolism and nutrition disorders	Zinc deficiency	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Musculoskeletal and connective tissue disorders	Total	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Arthralgia	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Osteochondrosis	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Nervous system disorders	Total	Patients with any TEAEs	3 (14.29)	2 (18.18)
			Patients with no TEAEs	18 (85.71)	9 (81.82)
			Threshold for subgroup analysis not reached		
		Disturbance in attention	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Dizziness	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Headache	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Nervous system disorders	Hyperammonaemic encephalopathy	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Lethargy	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Seizure	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Tonic convulsion	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Psychiatric disorders	Total	Patients with any TEAEs	2 (9.52)	1 (9.09)
			Patients with no TEAEs	19 (90.48)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Behaviour disorder	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Generalised anxiety disorder	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Panic attack	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Respiratory, thoracic and mediastinal disorders	Total	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Oropharyngeal pain	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Skin and subcutaneous tissue disorders	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Dry skin	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Skin and subcutaneous tissue disorders	Pruritus	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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4.10.16.1.35 Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Eye disorders	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Eye pain	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Ocular hyperaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Gastrointestinal disorders	Total	Patients with any TEAEs	2 (9.52)	3 (27.27)
			Patients with no TEAEs	19 (90.48)	8 (72.73)
			OR (95% CI)	0.28 (0.04, 2.01)	
			RR (95% CI)	0.35 (0.07, 1.79)	
			RD % (95% CI)	-17.75 (-46.91, 11.41)	
			p-value – Fisher's Exact Test	0.3098	
		Abdominal discomfort	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Abdominal pain	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Gastrointestinal disorders	Nausea	Patients with any TEAEs	0 (0.00)	3 (27.27)
			Patients with no TEAEs	21 (100.00)	8 (72.73)
			Threshold for subgroup analysis not reached		
		Vomiting	Patients with any TEAEs	2 (9.52)	2 (18.18)
			Patients with no TEAEs	19 (90.48)	9 (81.82)
			Threshold for subgroup analysis not reached		
	General disorders and administration site conditions	Total	Patients with any TEAEs	3 (14.29)	0 (0.00)
			Patients with no TEAEs	18 (85.71)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Illness	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	General disorders and administration site conditions	Peripheral swelling	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Pyrexia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Infections and infestations	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Gastrointestinal viral infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Infections and infestations	Respiratory syncytial virus infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Viral infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Injury, poisoning and procedural complications	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Contusion	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Injury, poisoning and procedural complications	Fall	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Procedural pain	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Investigations	Total	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Ammonia increased	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Investigations	Blood pressure increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Body temperature increased	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Metabolism and nutrition disorders	Total	Patients with any TEAEs	1 (4.76)	3 (27.27)
			Patients with no TEAEs	20 (95.24)	8 (72.73)
			Threshold for subgroup analysis not reached		
		Decreased appetite	Patients with any TEAEs	0 (0.00)	2 (18.18)
			Patients with no TEAEs	21 (100.00)	9 (81.82)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Metabolism and nutrition disorders	Hyperammonaemia	Patients with any TEAEs	1 (4.76)	2 (18.18)
			Patients with no TEAEs	20 (95.24)	9 (81.82)
			Threshold for subgroup analysis not reached		
	Musculoskeletal and connective tissue disorders	Total	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Pain in extremity	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Nervous system disorders	Total	Patients with any TEAEs	1 (4.76)	2 (18.18)
			Patients with no TEAEs	20 (95.24)	9 (81.82)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Nervous system disorders	Dizziness	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Headache	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Lethargy	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Psychiatric disorders	Total	Patients with any TEAEs	0 (0.00)	2 (18.18)
			Patients with no TEAEs	21 (100.00)	9 (81.82)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Psychiatric disorders	Generalised anxiety disorder	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Mood altered	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Respiratory, thoracic and mediastinal disorders	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Cough	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Respiratory, thoracic and mediastinal disorders	Rhinorrhoea	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Skin and subcutaneous tissue disorders	Total	Patients with any TEAEs	1 (4.76)	2 (18.18)
			Patients with no TEAEs	20 (95.24)	9 (81.82)
			Threshold for subgroup analysis not reached		
		Rash	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Skin exfoliation	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Vascular disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Hypertension	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
Non-US	Blood and lymphatic system disorders	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Anaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Blood and lymphatic system disorders	Iron deficiency anaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Eye disorders	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Eye irritation	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Eyelid oedema	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Gastrointestinal disorders	Total	Patients with any TEAEs	8 (38.10)	3 (27.27)
			Patients with no TEAEs	13 (61.90)	8 (72.73)
			OR (95% CI)	1.64 (0.33, 8.07)	
			RR (95% CI)	1.40 (0.46, 4.23)	
			RD % (95% CI)	10.82 (-22.70, 44.35)	
			p-value – Fisher's Exact Test	0.7026	
		Abdominal pain	Patients with any TEAEs	1 (4.76)	2 (18.18)
			Patients with no TEAEs	20 (95.24)	9 (81.82)
			Threshold for subgroup analysis not reached		
		Abdominal pain upper	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Gastrointestinal disorders	Anal rash	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Constipation	Patients with any TEAEs	3 (14.29)	1 (9.09)
			Patients with no TEAEs	18 (85.71)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Diarrhoea	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Haematochezia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Gastrointestinal disorders	Nausea	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Oral pain	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Vomiting	Patients with any TEAEs	4 (19.05)	1 (9.09)
			Patients with no TEAEs	17 (80.95)	10 (90.91)
			Threshold for subgroup analysis not reached		
	General disorders and administration site conditions	Total	Patients with any TEAEs	4 (19.05)	0 (0.00)
			Patients with no TEAEs	17 (80.95)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	General disorders and administration site conditions	Administration site extravasation	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Asthenia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Infusion site extravasation	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Oedema peripheral	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	General disorders and administration site conditions	Pyrexia	Patients with any TEAEs	3 (14.29)	0 (0.00)
			Patients with no TEAEs	18 (85.71)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Swelling face	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Hepatobiliary disorders	Total	Patients with any TEAEs	2 (9.52)	1 (9.09)
			Patients with no TEAEs	19 (90.48)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Cholelithiasis	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Hepatobiliary disorders	Hepatic cytolysis	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Immune system disorders	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Food allergy	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Hypersensitivity	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Infections and infestations	Total	Patients with any TEAEs	6 (28.57)	0 (0.00)
			Patients with no TEAEs	15 (71.43)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Conjunctivitis	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Fungal skin infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Influenza	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Infections and infestations	Nasopharyngitis	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Pharyngitis	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Upper respiratory tract infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Injury, poisoning and procedural complications	Total	Patients with any TEAEs	3 (14.29)	0 (0.00)
			Patients with no TEAEs	18 (85.71)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Injury, poisoning and procedural complications	Eye injury	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Fall	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Scratch	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Investigations	Total	Patients with any TEAEs	6 (28.57)	2 (18.18)
			Patients with no TEAEs	15 (71.43)	9 (81.82)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Investigations	Activated partial thromboplastin time prolonged	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Alanine aminotransferase increased	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Amino acid level increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Ammonia increased	Patients with any TEAEs	3 (14.29)	1 (9.09)
			Patients with no TEAEs	18 (85.71)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Investigations	Aspartate aminotransferase increased	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Blood alkaline phosphatase increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Blood potassium decreased	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Cardiac murmur	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Investigations	Electroencephalogram abnormal	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		International normalised ratio increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Prothrombin time prolonged	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Metabolism and nutrition disorders	Total	Patients with any TEAEs	2 (9.52)	1 (9.09)
			Patients with no TEAEs	19 (90.48)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Metabolism and nutrition disorders	Hyperammonaemia	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Hypokalaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Vitamin D deficiency	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Vitamin K deficiency	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Metabolism and nutrition disorders	Zinc deficiency	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Musculoskeletal and connective tissue disorders	Total	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Arthralgia	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Muscle spasms	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Musculoskeletal and connective tissue disorders	Osteochondrosis	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Nervous system disorders	Total	Patients with any TEAEs	4 (19.05)	1 (9.09)
			Patients with no TEAEs	17 (80.95)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Disturbance in attention	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Dizziness	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Nervous system disorders	Headache	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Hyperammonaemic encephalopathy	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Lethargy	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Seizure	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Nervous system disorders	Tonic convulsion	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Psychiatric disorders	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Behaviour disorder	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Panic attack	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Respiratory, thoracic and mediastinal disorders	Total	Patients with any TEAEs	3 (14.29)	2 (18.18)
			Patients with no TEAEs	18 (85.71)	9 (81.82)
			Threshold for subgroup analysis not reached		
		Cough	Patients with any TEAEs	2 (9.52)	1 (9.09)
			Patients with no TEAEs	19 (90.48)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Nasal congestion	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Nasal inflammation	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Respiratory, thoracic and mediastinal disorders	Oropharyngeal pain	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Skin and subcutaneous tissue disorders	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Dry skin	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Pruritus	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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4.10.16.1.36 Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Eye disorders	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Eye irritation	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Ocular hyperaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Gastrointestinal disorders	Total	Patients with any TEAEs	4 (19.05)	3 (27.27)
			Patients with no TEAEs	17 (80.95)	8 (72.73)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Gastrointestinal disorders	Abdominal pain	Patients with any TEAEs	1 (4.76)	2 (18.18)
			Patients with no TEAEs	20 (95.24)	9 (81.82)
			Threshold for subgroup analysis not reached		
		Abdominal pain upper	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Anal rash	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Constipation	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Gastrointestinal disorders	Diarrhoea	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Nausea	Patients with any TEAEs	1 (4.76)	2 (18.18)
			Patients with no TEAEs	20 (95.24)	9 (81.82)
			Threshold for subgroup analysis not reached		
		Vomiting	Patients with any TEAEs	2 (9.52)	1 (9.09)
			Patients with no TEAEs	19 (90.48)	10 (90.91)
			Threshold for subgroup analysis not reached		
	General disorders and administration site conditions	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	General disorders and administration site conditions	Administration site extravasation	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Infusion site extravasation	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Pyrexia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Hepatobiliary disorders	Total	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Hepatobiliary disorders	Hepatic cytolysis	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Immune system disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Hypersensitivity	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Infections and infestations	Total	Patients with any TEAEs	4 (19.05)	0 (0.00)
			Patients with no TEAEs	17 (80.95)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Infections and infestations	Influenza	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Nasopharyngitis	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Respiratory syncytial virus infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Upper respiratory tract infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Infections and infestations	Viral infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Injury, poisoning and procedural complications	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Contusion	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Fall	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Injury, poisoning and procedural complications	Procedural pain	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Investigations	Total	Patients with any TEAEs	4 (19.05)	1 (9.09)
			Patients with no TEAEs	17 (80.95)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Activated partial thromboplastin time prolonged	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Alanine aminotransferase increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Investigations	Amino acid level increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Aspartate aminotransferase increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Blood potassium decreased	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Blood pressure increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Investigations	Cardiac murmur	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Electroencephalogram abnormal	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		International normalised ratio increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Prothrombin time prolonged	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Metabolism and nutrition disorders	Total	Patients with any TEAEs	1 (4.76)	2 (18.18)
			Patients with no TEAEs	20 (95.24)	9 (81.82)
			Threshold for subgroup analysis not reached		
		Decreased appetite	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Hyperammonaemia	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Musculoskeletal and connective tissue disorders	Total	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Musculoskeletal and connective tissue disorders	Muscle spasms	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Pain in extremity	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Nervous system disorders	Total	Patients with any TEAEs	1 (4.76)	2 (18.18)
			Patients with no TEAEs	20 (95.24)	9 (81.82)
			Threshold for subgroup analysis not reached		
		Dizziness	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Nervous system disorders	Headache	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Hyperammonaemic encephalopathy	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Psychiatric disorders	Total	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Generalised anxiety disorder	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Psychiatric disorders	Panic attack	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Respiratory, thoracic and mediastinal disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Cough	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Skin and subcutaneous tissue disorders	Total	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Skin and subcutaneous tissue disorders	Rash	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Vascular disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Hypertension	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
≥ II	Blood and lymphatic system disorders	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Blood and lymphatic system disorders	Anaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Iron deficiency anaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Eye disorders	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Eye pain	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Eye disorders	Eyelid oedema	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Gastrointestinal disorders	Total	Patients with any TEAEs	6 (28.57)	3 (27.27)
			Patients with no TEAEs	15 (71.43)	8 (72.73)
			Threshold for subgroup analysis not reached		
		Abdominal discomfort	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Abdominal pain	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Gastrointestinal disorders	Constipation	Patients with any TEAEs	3 (14.29)	0 (0.00)
			Patients with no TEAEs	18 (85.71)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Diarrhoea	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Haematochezia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Nausea	Patients with any TEAEs	0 (0.00)	2 (18.18)
			Patients with no TEAEs	21 (100.00)	9 (81.82)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Gastrointestinal disorders	Oral pain	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Vomiting	Patients with any TEAEs	4 (19.05)	2 (18.18)
			Patients with no TEAEs	17 (80.95)	9 (81.82)
			Threshold for subgroup analysis not reached		
	General disorders and administration site conditions	Total	Patients with any TEAEs	5 (23.81)	0 (0.00)
			Patients with no TEAEs	16 (76.19)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Asthenia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	General disorders and administration site conditions	Illness	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Oedema peripheral	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Peripheral swelling	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Pyrexia	Patients with any TEAEs	3 (14.29)	0 (0.00)
			Patients with no TEAEs	18 (85.71)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	General disorders and administration site conditions	Swelling face	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Hepatobiliary disorders	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
			Patients with no TEAEs	19 (90.48)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Cholelithiasis	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Hepatic cytolysis	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Immune system disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Food allergy	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Infections and infestations	Total	Patients with any TEAEs	4 (19.05)	0 (0.00)
			Patients with no TEAEs	17 (80.95)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Conjunctivitis	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Infections and infestations	Fungal skin infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Gastrointestinal viral infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Nasopharyngitis	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Pharyngitis	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Injury, poisoning and procedural complications	Total	Patients with any TEAEs	3 (14.29)	0 (0.00)
			Patients with no TEAEs	18 (85.71)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Eye injury	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Fall	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Scratch	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Investigations	Total	Patients with any TEAEs	3 (14.29)	2 (18.18)
			Patients with no TEAEs	18 (85.71)	9 (81.82)
			Threshold for subgroup analysis not reached		
		Alanine aminotransferase increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Ammonia increased	Patients with any TEAEs	3 (14.29)	2 (18.18)
			Patients with no TEAEs	18 (85.71)	9 (81.82)
			Threshold for subgroup analysis not reached		
		Aspartate aminotransferase increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Investigations	Blood alkaline phosphatase increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Body temperature increased	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Metabolism and nutrition disorders	Total	Patients with any TEAEs	2 (9.52)	2 (18.18)
			Patients with no TEAEs	19 (90.48)	9 (81.82)
			Threshold for subgroup analysis not reached		
		Decreased appetite	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Metabolism and nutrition disorders	Hyperammonaemia	Patients with any TEAEs	1 (4.76)	2 (18.18)
			Patients with no TEAEs	20 (95.24)	9 (81.82)
			Threshold for subgroup analysis not reached		
		Hypokalaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Vitamin D deficiency	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Vitamin K deficiency	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Metabolism and nutrition disorders	Zinc deficiency	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Musculoskeletal and connective tissue disorders	Total	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Arthralgia	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Osteochondrosis	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Nervous system disorders	Total	Patients with any TEAEs	4 (19.05)	1 (9.09)
			Patients with no TEAEs	17 (80.95)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Disturbance in attention	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Dizziness	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Headache	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Nervous system disorders	Hyperammonaemic encephalopathy	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Lethargy	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Seizure	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Tonic convulsion	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Psychiatric disorders	Total	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Behaviour disorder	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Mood altered	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Respiratory, thoracic and mediastinal disorders	Total	Patients with any TEAEs	4 (19.05)	2 (18.18)
			Patients with no TEAEs	17 (80.95)	9 (81.82)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Respiratory, thoracic and mediastinal disorders	Cough	Patients with any TEAEs	3 (14.29)	1 (9.09)
			Patients with no TEAEs	18 (85.71)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Nasal congestion	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Nasal inflammation	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Oropharyngeal pain	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Respiratory, thoracic and mediastinal disorders	Rhinorrhoea	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Skin and subcutaneous tissue disorders	Total	Patients with any TEAEs	2 (9.52)	1 (9.09)
			Patients with no TEAEs	19 (90.48)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Dry skin	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Pruritus	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Any TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Skin and subcutaneous tissue disorders	Skin exfoliation	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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4.10.16.1.37 Any severe TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Investigations	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Aspartate aminotransferase increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Metabolism and nutrition disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Hyperammonaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any severe TEAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Psychiatric disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Panic attack	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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4.10.16.1.38 Any severe TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Investigations	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Aspartate aminotransferase increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Metabolism and nutrition disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Hyperammonaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Any severe TEAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Psychiatric disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Panic attack	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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4.10.16.1.39 Any severe TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Investigations	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Aspartate aminotransferase increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Metabolism and nutrition disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Hyperammonaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any severe TEAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Psychiatric disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Panic attack	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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4.10.16.1.40 Any severe TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Investigations	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Aspartate aminotransferase increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Metabolism and nutrition disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Hyperammonaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Any severe TEAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Psychiatric disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Panic attack	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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4.10.16.1.41 Treatment emergent SAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Male	Gastrointestinal disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Vomiting	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Metabolism and nutrition disorders	Total	Patients with any TEAEs	1 (4.76)	2 (18.18)
			Patients with no TEAEs	20 (95.24)	9 (81.82)
			Threshold for subgroup analysis not reached		
		Hyperammonaemia	Patients with any TEAEs	1 (4.76)	2 (18.18)
			Patients with no TEAEs	20 (95.24)	9 (81.82)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Treatment emergent SAEs by SOC and PT by gender

Gender	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Female	Metabolism and nutrition disorders	Total	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Hyperammonaemia	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Nervous system disorders	Total	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Hyperammonaemic encephalopathy	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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4.10.16.1.42 Treatment emergent SAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
<10.5 years old at screening	Gastrointestinal disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Vomiting	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Metabolism and nutrition disorders	Total	Patients with any TEAEs	0 (0.00)	2 (18.18)
			Patients with no TEAEs	21 (100.00)	9 (81.82)
			Threshold for subgroup analysis not reached		
		Hyperammonaemia	Patients with any TEAEs	0 (0.00)	2 (18.18)
			Patients with no TEAEs	21 (100.00)	9 (81.82)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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Treatment emergent SAEs by SOC and PT by age group

Age Group	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ 10.5 years old at screening	Metabolism and nutrition disorders	Total	Patients with any TEAEs	2 (9.52)	1 (9.09)
			Patients with no TEAEs	19 (90.48)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Hyperammonaemia	Patients with any TEAEs	2 (9.52)	1 (9.09)
			Patients with no TEAEs	19 (90.48)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Nervous system disorders	Total	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Hyperammonaemic encephalopathy	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Median age used as cut-off point.
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4.10.16.1.43 Treatment emergent SAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
US	Metabolism and nutrition disorders	Total	Patients with any TEAEs	1 (4.76)	2 (18.18)
			Patients with no TEAEs	20 (95.24)	9 (81.82)
			Threshold for subgroup analysis not reached		
		Hyperammonaemia	Patients with any TEAEs	1 (4.76)	2 (18.18)
			Patients with no TEAEs	20 (95.24)	9 (81.82)
			Threshold for subgroup analysis not reached		
Non-US	Gastrointestinal disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Vomiting	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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Treatment emergent SAEs by SOC and PT by region

Region	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Non-US	Metabolism and nutrition disorders	Total	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Hyperammonaemia	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Nervous system disorders	Total	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Hyperammonaemic encephalopathy	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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4.10.16.1.44 Treatment emergent SAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
I	Metabolism and nutrition disorders	Total	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Hyperammonaemia	Patients with any TEAEs	1 (4.76)	1 (9.09)
			Patients with no TEAEs	20 (95.24)	10 (90.91)
			Threshold for subgroup analysis not reached		
	Nervous system disorders	Total	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		
		Hyperammonaemic encephalopathy	Patients with any TEAEs	0 (0.00)	1 (9.09)
			Patients with no TEAEs	21 (100.00)	10 (90.91)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Treatment emergent SAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Gastrointestinal disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Vomiting	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
	Metabolism and nutrition disorders	Total	Patients with any TEAEs	1 (4.76)	2 (18.18)
			Patients with no TEAEs	20 (95.24)	9 (81.82)
			Threshold for subgroup analysis not reached		
		Hyperammonaemia	Patients with any TEAEs	1 (4.76)	2 (18.18)
			Patients with no TEAEs	20 (95.24)	9 (81.82)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

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Treatment emergent SAEs by SOC and PT by GMFCS level at baseline

GMFCS at Baseline	Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
≥ II	Nervous system disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		
		Hyperammonaemic encephalopathy	Patients with any TEAEs	1 (4.76)	0 (0.00)
			Patients with no TEAEs	20 (95.24)	11 (100.00)
			Threshold for subgroup analysis not reached		

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
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4.10.16.2 Gesamtraten bereinigt um krankheitsbezogene Ereignisse

4.10.16.2.1 Patients with at least one TEAE while excluding disease associated adverse events

Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Patients with any TEAEs	18 (85.71)	10 (90.91)
Patients with no TEAEs	3 (14.29)	1 (9.09)
OR (95% CI)	0.60 (0.05, 6.56)	
RR (95% CI)	0.94 (0.73, 1.22)	
RD % (95% CI)	-5.19 (-27.84, 17.45)	
p-value – Fisher's Exact Test	1.0000	

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.

Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.

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4.10.16.2.2 Patients with at least one severe TEAE while excluding disease associated adverse events

Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Patients with any severe TEAEs	1 (4.76)	0 (0.00)
Patients with no severe TEAEs	20 (95.24)	11 (100.00)
OR (95% CI)	1.68 (0.06, 44.77)	
RR (95% CI)	1.64 (0.07, 37.15)	
RD % (95% CI)	2.65 (-12.80, 18.10)	
p-value – Fisher's Exact Test	1.0000	

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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4.10.16.2.3 Patients with at least one treatment emergent SAE while excluding disease associated adverse events

Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Patients with any treatment emergent SAEs	1 (4.76)	0 (0.00)
Patients with no treatment emergent SAEs	20 (95.24)	11 (100.00)
OR (95% CI)	1.68 (0.06, 44.77)	
RR (95% CI)	1.64 (0.07, 37.15)	
RD % (95% CI)	2.65 (-12.80, 18.10)	
p-value – Fisher's Exact Test	1.0000	

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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4.10.16.2.4 Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Blood and lymphatic system disorders	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
		Patients with no TEAEs	19 (90.48)	11 (100.00)
	Anaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Iron deficiency anaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
Eye disorders	Total	Patients with any TEAEs	4 (19.05)	0 (0.00)
		Patients with no TEAEs	17 (80.95)	11 (100.00)
		OR (95% CI)	5.91 (0.29, 120.58)	
		RR (95% CI)	4.91 (0.29, 83.67)	
		RD % (95% CI)	16.29 (-4.01, 36.58)	
		p-value – Fisher's Exact Test	0.2720	
	Eye irritation	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Eye disorders	Eye pain	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Eyelid oedema	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Ocular hyperaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
Gastrointestinal disorders	Total	Patients with any TEAEs	10 (47.62)	6 (54.55)
		Patients with no TEAEs	11 (52.38)	5 (45.45)
		OR (95% CI)	0.76 (0.18, 3.27)	
		RR (95% CI)	0.87 (0.43, 1.76)	
		RD % (95% CI)	-6.93 (-43.29, 29.43)	
		p-value – Fisher's Exact Test	1.0000	
	Abdominal discomfort	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Gastrointestinal disorders	Abdominal pain	Patients with any TEAEs	1 (4.76)	3 (27.27)
		Patients with no TEAEs	20 (95.24)	8 (72.73)
		OR (95% CI)	0.13 (0.01, 1.48)	
		RR (95% CI)	0.17 (0.02, 1.49)	
		RD % (95% CI)	-22.51 (-50.36, 5.34)	
		p-value – Fisher's Exact Test	0.1055	
	Abdominal pain upper	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Anal rash	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Gastrointestinal disorders	Constipation	Patients with any TEAEs	3 (14.29)	1 (9.09)
		Patients with no TEAEs	18 (85.71)	10 (90.91)
		OR (95% CI)	1.67 (0.15, 18.22)	
		RR (95% CI)	1.57 (0.18, 13.39)	
		RD % (95% CI)	5.19 (-17.45, 27.84)	
		p-value – Fisher's Exact Test	1.0000	
	Diarrhoea	Patients with any TEAEs	1 (4.76)	1 (9.09)
		Patients with no TEAEs	20 (95.24)	10 (90.91)
	Haematochezia	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Gastrointestinal disorders	Nausea	Patients with any TEAEs	1 (4.76)	4 (36.36)
		Patients with no TEAEs	20 (95.24)	7 (63.64)
		OR (95% CI)	0.09 (0.01, 0.92)	
		RR (95% CI)	0.13 (0.02, 1.03)	
		RD % (95% CI)	-31.60 (-61.45, -1.75)	
		p-value – Fisher's Exact Test	0.0367 ***	
	Oral pain	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Vomiting	Patients with any TEAEs	6 (28.57)	3 (27.27)
		Patients with no TEAEs	15 (71.43)	8 (72.73)
		OR (95% CI)	1.07 (0.21, 5.44)	
		RR (95% CI)	1.05 (0.32, 3.40)	
		RD % (95% CI)	1.30 (-31.35, 33.95)	
		p-value – Fisher's Exact Test	1.0000	

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.

NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.

Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.

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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
General disorders and administration site conditions	Total	Patients with any TEAEs	7 (33.33)	0 (0.00)
		Patients with no TEAEs	14 (66.67)	11 (100.00)
		OR (95% CI)	11.90 (0.61, 230.84)	
		RR (95% CI)	8.18 (0.51, 131.22)	
		RD % (95% CI)	29.92 (7.12, 52.73)	
		p-value – Fisher's Exact Test	0.0664	
	Administration site extravasation	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Asthenia	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Illness	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Infusion site extravasation	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
General disorders and administration site conditions	Oedema peripheral	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Peripheral swelling	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Pyrexia	Patients with any TEAEs	4 (19.05)	0 (0.00)
		Patients with no TEAEs	17 (80.95)	11 (100.00)
		OR (95% CI)	5.91 (0.29, 120.58)	
		RR (95% CI)	4.91 (0.29, 83.67)	
		RD % (95% CI)	16.29 (-4.01, 36.58)	
		p-value – Fisher's Exact Test	0.2720	
	Swelling face	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
Hepatobiliary disorders	Total	Patients with any TEAEs	2 (9.52)	1 (9.09)
		Patients with no TEAEs	19 (90.48)	10 (90.91)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Hepatobiliary disorders	Cholelithiasis	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Hepatic cytolysis	Patients with any TEAEs	1 (4.76)	1 (9.09)
		Patients with no TEAEs	20 (95.24)	10 (90.91)
Immune system disorders	Total	Patients with any TEAEs	2 (9.52)	0 (0.00)
		Patients with no TEAEs	19 (90.48)	11 (100.00)
	Food allergy	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Hypersensitivity	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Infections and infestations	Total	Patients with any TEAEs	8 (38.10)	0 (0.00)
		Patients with no TEAEs	13 (61.90)	11 (100.00)
		OR (95% CI)	14.48 (0.75, 279.08)	
		RR (95% CI)	9.27 (0.58, 147.11)	
		RD % (95% CI)	34.47 (11.19, 57.75)	
		p-value – Fisher's Exact Test	0.0292 ***	
	Conjunctivitis	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Fungal skin infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Gastrointestinal viral infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Influenza	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Infections and infestations	Nasopharyngitis	Patients with any TEAEs	2 (9.52)	0 (0.00)
		Patients with no TEAEs	19 (90.48)	11 (100.00)
	Pharyngitis	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Respiratory syncytial virus infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Upper respiratory tract infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Viral infection	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Injury, poisoning and procedural complications	Total	Patients with any TEAEs	5 (23.81)	0 (0.00)
		Patients with no TEAEs	16 (76.19)	11 (100.00)
		OR (95% CI)	7.67 (0.39, 152.66)	
		RR (95% CI)	6.00 (0.36, 99.49)	
		RD % (95% CI)	20.83 (-0.50, 42.17)	
		p-value – Fisher's Exact Test	0.1378	
	Contusion	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Eye injury	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Fall	Patients with any TEAEs	2 (9.52)	0 (0.00)
		Patients with no TEAEs	19 (90.48)	11 (100.00)
	Procedural pain	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Injury, poisoning and procedural complications	Scratch	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
Investigations	Total	Patients with any TEAEs	5 (23.81)	2 (18.18)
		Patients with no TEAEs	16 (76.19)	9 (81.82)
		OR (95% CI)	1.41 (0.23, 8.78)	
		RR (95% CI)	1.31 (0.30, 5.69)	
		RD % (95% CI)	5.63 (-23.55, 34.81)	
		p-value – Fisher's Exact Test	1.0000	
	Activated partial thromboplastin time prolonged	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Amino acid level increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Blood alkaline phosphatase increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Investigations	Blood potassium decreased	Patients with any TEAEs	0 (0.00)	1 (9.09)
		Patients with no TEAEs	21 (100.00)	10 (90.91)
	Blood pressure increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Body temperature increased	Patients with any TEAEs	0 (0.00)	1 (9.09)
		Patients with no TEAEs	21 (100.00)	10 (90.91)
	Cardiac murmur	Patients with any TEAEs	1 (4.76)	1 (9.09)
		Patients with no TEAEs	20 (95.24)	10 (90.91)
	Electroencephalogram abnormal	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	International normalised ratio increased	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Prothrombin time prolonged	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Metabolism and nutrition disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Hypokalaemia	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Vitamin D deficiency	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Vitamin K deficiency	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Zinc deficiency	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Musculoskeletal and connective tissue disorders	Total	Patients with any TEAEs	1 (4.76)	2 (18.18)
		Patients with no TEAEs	20 (95.24)	9 (81.82)
		OR (95% CI)	0.23 (0.02, 2.81)	
		RR (95% CI)	0.26 (0.03, 2.58)	
		RD % (95% CI)	-13.42 (-37.97, 11.13)	
		p-value – Fisher's Exact Test	0.2661	
	Arthralgia	Patients with any TEAEs	0 (0.00)	1 (9.09)
		Patients with no TEAEs	21 (100.00)	10 (90.91)
	Muscle spasms	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Osteochondrosis	Patients with any TEAEs	0 (0.00)	1 (9.09)
		Patients with no TEAEs	21 (100.00)	10 (90.91)
	Pain in extremity	Patients with any TEAEs	0 (0.00)	1 (9.09)
		Patients with no TEAEs	21 (100.00)	10 (90.91)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Nervous system disorders	Total	Patients with any TEAEs	4 (19.05)	2 (18.18)
		Patients with no TEAEs	17 (80.95)	9 (81.82)
		OR (95% CI)	1.06 (0.16, 6.94)	
		RR (95% CI)	1.05 (0.23, 4.85)	
		RD % (95% CI)	0.87 (-27.45, 29.18)	
		p-value – Fisher's Exact Test	1.0000	
	Disturbance in attention	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Dizziness	Patients with any TEAEs	2 (9.52)	0 (0.00)
		Patients with no TEAEs	19 (90.48)	11 (100.00)
	Headache	Patients with any TEAEs	2 (9.52)	1 (9.09)
		Patients with no TEAEs	19 (90.48)	10 (90.91)
	Lethargy	Patients with any TEAEs	1 (4.76)	1 (9.09)
		Patients with no TEAEs	20 (95.24)	10 (90.91)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Psychiatric disorders	Total	Patients with any TEAEs	2 (9.52)	2 (18.18)
		Patients with no TEAEs	19 (90.48)	9 (81.82)
		OR (95% CI)	0.47 (0.06, 3.92)	
		RR (95% CI)	0.52 (0.08, 3.23)	
		RD % (95% CI)	-8.66 (-34.68, 17.36)	
		p-value – Fisher's Exact Test	0.5932	
	Behaviour disorder	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Generalised anxiety disorder	Patients with any TEAEs	0 (0.00)	1 (9.09)
		Patients with no TEAEs	21 (100.00)	10 (90.91)
	Mood altered	Patients with any TEAEs	0 (0.00)	1 (9.09)
		Patients with no TEAEs	21 (100.00)	10 (90.91)
	Panic attack	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Respiratory, thoracic and mediastinal disorders	Total	Patients with any TEAEs	5 (23.81)	2 (18.18)
		Patients with no TEAEs	16 (76.19)	9 (81.82)
		OR (95% CI)	1.41 (0.23, 8.78)	
		RR (95% CI)	1.31 (0.30, 5.69)	
		RD % (95% CI)	5.63 (-23.55, 34.81)	
		p-value – Fisher's Exact Test	1.0000	
	Cough	Patients with any TEAEs	4 (19.05)	1 (9.09)
		Patients with no TEAEs	17 (80.95)	10 (90.91)
		OR (95% CI)	2.35 (0.23, 24.10)	
		RR (95% CI)	2.10 (0.27, 16.54)	
		RD % (95% CI)	9.96 (-13.93, 33.85)	
		p-value – Fisher's Exact Test	0.6367	
	Nasal congestion	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.

Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.

NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.

Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.

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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Respiratory, thoracic and mediastinal disorders	Nasal inflammation	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Oropharyngeal pain	Patients with any TEAEs	1 (4.76)	1 (9.09)
		Patients with no TEAEs	20 (95.24)	10 (90.91)
	Rhinorrhoea	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
Skin and subcutaneous tissue disorders	Total	Patients with any TEAEs	3 (14.29)	2 (18.18)
		Patients with no TEAEs	18 (85.71)	9 (81.82)
		OR (95% CI)	0.75 (0.11, 5.32)	
		RR (95% CI)	0.79 (0.15, 4.03)	
		RD % (95% CI)	-3.90 (-31.16, 23.37)	
		p-value – Fisher's Exact Test	1.0000	
	Dry skin	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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Any TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Skin and subcutaneous tissue disorders	Pruritus	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Rash	Patients with any TEAEs	1 (4.76)	1 (9.09)
		Patients with no TEAEs	20 (95.24)	10 (90.91)
	Skin exfoliation	Patients with any TEAEs	0 (0.00)	1 (9.09)
		Patients with no TEAEs	21 (100.00)	10 (90.91)
Vascular disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Hypertension	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=3; Placebo n=2.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
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4.10.16.2.5 Any severe TEAEs by SOC and PT while excluding disease associated adverse events

Primary System Organ Class	Dictionary-Derived Term	Statistic	Pegzilarginase (N = 21) n (%)	Placebo (N = 11) n (%)
Psychiatric disorders	Total	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)
	Panic attack	Patients with any TEAEs	1 (4.76)	0 (0.00)
		Patients with no TEAEs	20 (95.24)	11 (100.00)

Abbreviations: TEAE = Treatment-emerged Adverse Event; CI = Confidence Interval; N = Number of patients in the analysis; n = number of patients with ≥ 1 event; OR = Odd Ratio; RD = Risk Difference; RR = Risk Ratio.
Minimum event number in at least one of the study arms for AE analyses by SOC and PT: Pegzilarginase n=2; Placebo n=1.
NOTE: Zero cell correction performed: in the event of zero cells, the correction value of 0.5 added to each cell frequency of the corresponding fourfold table.
Disease associated events: Ammonia increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperammonaemia, Decreased appetite, Hyperammonaemic encephalopathy, Seizure and Tonic convulsion.
Program: t-teae-soc-sens.sas
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