**Supplemental Table 1. Summary of Clinical Outcome Data in the Full Population**

|  |  |  |
| --- | --- | --- |
| **Assessment** |  | **All Subjects** |
| **Baseline**  | **Month 6** | **Month 12** | **Month 24** | **Month 36** |
| **HHD UE composite score, kg** |  |  |  |  |  |
| Mean (SD) [n] | 34.3 (32.0) [95] | 34.1 (32.7) [85] | 33.2 (33.2) [84) | 30.5 (31.0) [72] | 29.4 (32.6) [49] |
| Mean (SD) change from baseline [n] | — | –0.6 (3.6) [85] | –1.7 (5.5) [84] | –3.5 (6.7) [71] | –3.7 (8.0) [48] |
| LSM (95% CI) change from baseline | — | –0.5 (–1.3, 0.2) | –1.8 (–2.9, –0.6) | –3.4 (–4.8, –1.9) | –3.8 (–5.9, –1.7) |
| *P* value | — | 0.1695 | 0.0023 | <0.001 | 0.0005 |
| **HHD LE composite score, kg** |  |  |  |  |  |
| Mean (SD) [n] | 32.0 (34.1) [86] | 30.9 (34.0) [82] | 30.2 (33.4) [80] | 27.2 (33.4) [69] | 25.5 (31.2) [49] |
| Mean (SD) change from baseline [n] | — | –1.2 (6.0) [79] | –2.3 (7.5) [78] | –3.9 (8.6) [66] | –5.3 (11.5) [46] |
| LSM (95% CI) change from baseline | — | –1.0 (–2.3, 0.2) | –2.3 (–3.7, –0.9) | –4.1 (–6.0, –2.2) | –4.9 (–7.7, –2.2) |
| *P* value | — | 0.0986 | 0.0019 | <0.0001 | 0.0005 |
| **GNEM-FAS total score (≥200 m)** |  |  |  |  |  |
| Mean (SD) [n] | 83.6 (12.5) [40] | 83.3 (13.2) [39] | 82.2 (13.4) [38] | 79.5 (12.9) [31] | 77.9 (14.6) [26] |
| Mean (SD) change from baseline [n] | — | 0.1 (5.2) [39] | –1.4 (5.8) [38] | –3.7 (8.0) [31] | –5.7 (8.8) [26] |
| LSM (95% CI) change from baseline | — | 0.1 (–1.6, 1.7) | –1.3 (–3.1, 0.5) | –3.9 (–6.4, –1.4) | –6.3 (–9.4, –3.2) |
| *P* value | — | 0.9333 | 0.1619 | 0.0023 | <0.0001 |
| **GNEM-FAS total score (<200 m)** |  |  |  |  |  |
| Mean (SD) [n] | 72.5 (14.1) [17] | 72.2 (16.2) [16] | 70.8 (16.0) [16] | 65.0 (13.5) [13] | 56.7 (14.2) [12] |
| Mean (SD) change from baseline [n] | — | –1.0 (8.3) [16] | –2.4 (8.7) [16] | –7.3 (8.5) [13] | –13.6 (11.7) [12] |
| LSM (95% CI) change from baseline | — | –0.9 (–4.9, 3.1) | –2.3 (–6.5, 1.8) | –5.9 (–10.0, –1.8) | –12.3 (–18.3, –6.3) |
| *P* value | — | 0.6610 | 0.2694 | 0.0049 | <0.0001 |
| **GNEM-FAS mobility score (≥200 m)** |  |  |  |  |  |
| Mean (SD) [n] | 29.0 (7.7) [40] | 28.9 (7.8) [39] | 28.1 (7.6) [38] | 26.7 (7.4) [31] | 26.0 (7.8) [26] |
| Mean (SD) change from baseline [n] | — | 0.2 (2.5) [39] | –0.8 (3.3) [38] | –1.9 (4.2) [31] | –2.6 (5.0) [26] |
| LSM (95% CI) change from baseline | — | 0.2 (–0.6, 1.0) | –0.7 (–1.7, 0.3) | –1.9 (–3.2, –0.6) | –2.8 (–4.5, –1.2) |
| *P* value | — | 0.6628 | 0.1565 | 0.0036 | 0.0007 |
| **GNEM-FAS mobility score (<200 m)** |  |  |  |  |  |
| Mean (SD) [n] | 25.1 (5.2) [17] | 23.7 (6.4) [16] | 23.1 (6.4) [16] | 21.4 (4.7) [13] | 18.2 (5.3) [12] |
| Mean (SD) change from baseline [n] | — | –1.3 (4.3) [16] | –1.9 (4.4) [16] | –3.5 (4.2) [13] | –6.0 (6.7) [12] |
| LSM (95% CI) change from baseline | — | –1.2 (–3.3, 0.8) | –1.8 (–3.9, 0.2) | –3.1 (–4.9, –1.2) | –5.7 (–8.9, –2.5) |
| *P* value | — | 0.2467 | 0.0780 | 0.0010 | 0.0005 |
| **GNEM-FAS UE score (≥200 m), kg** |  |  |  |  |  |
| Mean (SD) [n] | 29.5 (3.3) [40] | 29.0 (4.2) [39] | 29.0 (4.1) [38] | 28.4 (3.9) [31] | 28.2 (4.5) [26] |
| Mean (SD) change from baseline [n] | — | –0.4 (2.0) [39] | –0.5 (2.1) [38] | –1.2 (2.7) [31] | –1.6 (2.8) [26] |
| LSM (95% CI) change from baseline | — | –0.4 (–1.0, 0.2) | –4.6 (–1.1, 0.2) | –1.2 (–2.1, –0.3) | –1.8 (–2.9, –0.7) |
| *P* value | — | 0.1880 | 0.1720 | 0.0070 | 0.0009 |
| **GNEM-FAS UE score (<200 m), kg** |  |  |  |  |  |
| Mean (SD) [n] | 25.5 (5.1) [17] | 25.9 (5.5) [16] | 25.8 (5.8) [16] | 23.7 (5.3) [13] | 20.8 (6.0) [12] |
| Mean (SD) change from baseline [n] | — | 0.1 (2.6) [16] | 0 (3.0) [16] | –1.5 (3.5) [13] | –3.4 (3.9) [12] |
| LSM (95% CI) change from baseline | — | 0.1 (–1.2, 1.5) | 0.02 (–1.5, 1.5) | –1.0 (–2.8, 0.8) | –3.1 (–5.1, –1.0) |
| *P* value | — | 0.8332 | 0.9822 | 0.2659 | 0.0033 |
| **GNEM-FAS self-care score (≥200 m)** |  |  |  |  |  |
| Mean (SD) [n] | 25.2 (3.0) [40] | 25.4 (2.9) [39] | 25.1 (3.3) [38] | 24.5 (3.1) [31] | 23.7 (4.2) [26] |
| Mean (SD) change from baseline [n] | — | 0.3 (2.2) [39] | –0.1 (2.1) [38] | –0.7 (2.7) [31] | –1.5 (2.7) [26] |
| LSM (95% CI) change from baseline | — | 0.3 (–0.3, 1.0) | –0.1 (–0.7, 0.5) | –0.7 (–1.5, 0.1) | –1.6 (–2.6, –0.6) |
| *P* value | — | 0.3274 | 0.7726 | 0.0965 | 0.0015 |
| **GNEM-FAS self-care score (<200 m)** |  |  |  |  |  |
| Mean (SD) [n] | 22.0 (5.6) | 22.6 (6.2) [16] | 21.9 (5.4) [16] | 19.9 (5.4) [13] | 17.6 (4.8) [12] |
| Mean (SD) change from baseline [n] | — | 0.1 (3.4) [16] | –0.6 (2.9) [16] | –2.4 (3.1) [13] | –4.1 (4.0) [12] |
| LSM (95% CI) change from baseline | — | 0.2 (–1.5, 1.9) | –0.5 (–1.8, 0.8) | –1.9 (–3.4, –0.4) | –3.7 (–5.6, –1.7) |
| *P* value | — | 0.8281 | 0.4585 | 0.0150 | 0.0003 |
| **6MWT, m** |  |  |  |  |  |
| Mean (SD) [n] | 311.4 (147.6) [43] | 331.3 (144.5) [40] | 337.4 (137.6) [40] | 325.9 (148.6) [38] | 353.0 (140.0) [28] |
| Mean (SD) change from baseline [n] | — | 3.3 (43.0) [40] | 9.4 (48.5) [40] | –2.2 (61.7) [38] | 8.6 (65.0) [28] |
| LSM (95% CI) change from baseline | — | 3.3 (–9.9, 16.5) | 9.3 (–5.2, 23.9) | –1.2 (–20.0, 17.7) | 7.1 (–15.9, 30.1) |
| *P* value | — | 0.6249 | 0.2094 | 0.9025 | 0.5460 |
| **6MWT (≥200 m), m** |  |  |  |  |  |
| Mean (SD) [n] | 387.6 (105.5) [30] | 393.8 (104.0) [30] | 395.1 (101.8) [30] | 389.2 (111.9) [28] | 380.5 (127.5) [24] |
| Mean (SD) change from baseline [n] | — | 6.2 (41.5) [30] | 7.5 (47.4) [30] | –2.8 (60.4) [28] | 3.2 (60.9) [24] |
| LSM (95% CI) change from baseline | — | 6.1 (–8.3, 20.4) | 7.4 (–8.7, 23.4) | –1.5 (–22.6, 19.6) | 3.2 (–20.4, 26.8) |
| *P* value | — | 0.4070 | 0.3681 | 0.8885 | 0.7908 |
| **6MWT (<200 m), m** |  |  |  |  |  |
| Mean (SD) [n] | 135.5 (36.9) [13] | 143.7 (58.8) [10] | 164.0 (64.5) [10] | 148.5 (76.3) [10] | 188.0 (97.5) [4] |
| Mean (SD) change from baseline [n] | — | –5.4 (48.6) [10] | 14.9 (53.9) [10] | –0.6 (68.3) [10] | 41.0 (89.3) [4] |
| LSM (95% CI) change from baseline | — | –5.4 (–32.7, 21.9) | 14.9 (–15.1, 44.9) | –0.6 (–39.7, 38.5) | 27.1 (–30.9, 85.2) |
| *P* value | — | 0.6983 | 0.3297 | 0.9760 | 0.3599 |
| **6MWT (% predicted distance)** |  |  |  |  |  |
| Mean (SD) [n] | 43.1 (19.1) [43] | 46.0 (18.8) [40] | 46.8 (17.8) [40] | 45.2 (19.8) [38] | 48.9 (18.6) [28] |
| Mean (SD) change from baseline [n] | — | 0.5 (5.9) [40] | 1.4 (6.7) [40] | –0.2 (8.6) [38] | 1.2 (9.0) [28] |
| LSM (95% CI) change from baseline | — | 0.5 (–1.3, 2.3) | 1.4 (–0.7, 3.4) | –0.02, (–2.6, 2.6) | 1.0 (–2.2, 4.1) |
| *P* value | — | 0.5799 | 0.1842 | 0.9903 | 0.5546 |
| **6MWT (% predicted distance, ≥200 m)** |  |  |  |  |  |
| Mean (SD) [n] | 53.2 (12.8) [30] | 54.1 (13.2) [30] | 54.3 (12.8) [30] | 53.5 (15.0) [28] | 52.5 (16.9) [24] |
| Mean (SD) change from baseline [n] | — | 0.9 (5.6) [30] | 1.1 (6.5) [30] | –0.1 (8.2) [28] | 0.4 (8.3) [24] |
| LSM (95% CI) change from baseline | — | 0.9 (–1.0, 2.9) | 1.1 (–1.1, 3.3) | 0.1 (–2.9, 3.0) | 0.4 (–2.8, 3.3) |
| *P* value | — | 0.3546 | 0.3284 | 0.9701 | 0.7954 |
| **6MWT (% predicted distance, <200 m)** |  |  |  |  |  |
| Mean (SD) [n] | 19.7 (6.2) [13] | 21.4 (8.9) [10] | 24.3 (9.4) [10] | 21.9 (10.8) [10] | 27.3 (13.8) [4] |
| Mean (SD) change from baseline [n] | — | –0.8 (7.0) [10] | 2.2 (7.7) [10] | –0.3 (10.0) [10] | 5.8 (13.0) [4] |
| LSM (95% CI) change from baseline | — | –0.8 (–4.7, 3.2) | 2.2 (–2.3, 6.6) | –0.3 (–6.1, 5.6) | 3.7 (–5.1, 12.5) |
| *P* value | — | 0.7090 | 0.3350 | 0.9335 | 0.4088 |

6MWT, six-minute walk test; GNEM-FAS, GNE myopathy functional activity scale; HHD, hand-held dynamometry; LE, lower extremity; UE, upper extremity.

**Supplemental Table 2. Summary of Clinical Outcome Data in Bulgarian (n=47) and Non-Bulgarian (n=48) Subjects**

|  |  |  |
| --- | --- | --- |
| **Assessment** |  | **All Subjects** |
| **Baseline**  | **Month 6** | **Month 12** | **Month 24** | **Month 36** |
| **Bulgarian HHD UE composite score, kg** |  |  |  |  |  |
| Mean (SD) [n] | 23.1 (24.5) [47] | 21.5 (23.5) [42] | 20.0 (22.7) [42] | 16.2 (20.7) [37] | 15.1 (21.8) [28] |
| Mean (SD) change from baseline [n] | — | –0.8 (3.1) [42] | –2.0 (4.0) ]42] | –3.3 (5.4) [37] | –2.6 (7.0) [28] |
| LSM (95% CI) change from baseline | — | –0.7 (–1.6, 0.3) | –2.0 (–3.0, –0.9) | –3.0 (–4.5, –1.4) | –2.9 (–5.2, –0.6) |
| *P* value | — | 0.1613 | 0.0002 | 0.0002 | 0.0145 |
| **Non-Bulgarian HHD UE composite score, kg** |  |  |  |  |  |
| Mean (SD) [n] | 45.8 (34.8) [46] | 46.4 (35.8) [43] | 46.4 (36.9) [42] | 45.7 (33.0) [35] | 48.5 (35.1) [21] |
| Mean (SD) change from baseline [n] | — | –0.3 (4.1) [43] | –1.4 (6.7) [42] | –3.7 (8.0) [34] | –5.3 (9.1) [20] |
| LSM (95% CI) change from baseline | — | –0.3 (–1.5, 1.0) | –1.5 (–3.5, 0.6) | –3.7 (–6.3, –1.2) | –5.1 (–8.8, –1.3) |
| *P* value | — | 0.6604 | 0.1594 | 0.0045 | 0.0085 |
| **Bulgarian HHD LE composite score, kg** |  |  |  |  |  |
| Mean (SD) [n] | 20.4 (22.0) [42] | 18.8 (22.7) [39] | 18.6 (22.6) [39] | 12.8 (16.0) [33] | 12.8 (17.6) [26] |
| Mean (SD) change from baseline [n] | — | –1.3 (3.8) [38] | –1.6 (4.5) [38] | –3.1 (4.6) [32] | –1.2 (4.8) [25] |
| LSM (95% CI) change from baseline | — | –1.3 (–2.4, –0.2) | –1.6 (–2.9, –0.3) | –2.8 (–4.4, –1.3) | –1.5 (–3.4, 0.3) |
| *P* value | — | 0.0240 | 0.0196 | 0.0002 | 0.1028 |
| **Non-Bulgarian HHD LE composite score, kg** |  |  |  |  |  |
| Mean (SD) [n] | 43.1 (39.8) [44] | 41.8 (38.9) [43] | 41.3 (38.3) [41] | 40.4 (39.4) [36] | 39.8 (37.0) [23] |
| Mean (SD) change from baseline [n] | — | –1.0 (7.6) [41] | –3.0 (9.5) [40] | –4.6 (11.2) [34] | –10.2 (14.9) [21] |
| LSM (95% CI) change from baseline | — | –0.9 (–3.2, 1.3) | –3.1 (–5.8, –0.5) | –5.5 (–9.0, –1.9) | –8.8 (–14.0, –3.6) |
| *P* value | — | 0.4155 | 0.0197 | 0.0024 | 0.0009 |
| **Bulgarian GNEM-FAS total score (≥200 m)** |  |  |  |  |  |
| Mean (SD) [n] | 84.4 (12.7) [12] | 84.2 (13.6) [12] | 83.4 (12.7) [12] | 79.5 (14.7) [8] | 83.7 (14.3) [6] |
| Mean (SD) change from baseline [n] | — | –0.3 (4.3) [12] | –1.0 (6.0) [12] | –4.9 (8.1) [8] | –1.2 (7.4) [6] |
| LSM (95% CI) change from baseline | — | –0.2 (–2.7, 2.2) | –1.0 (–4.3, 2.3) | –4.7 (–9.0, –0.3) | –2.0 (–5.9, 1.9) |
| *P* value | — | 0.8493 | 0.5545 | 0.0356 | 0.3134 |

GNEM-FAS, GNE myopathy functional activity scale; HHD, hand-held dynamometry; LE, lower extremity; UE, upper extremity.

**Supplemental Table 3. Changes in GNE Myopathy-related Symptoms**

|  |  |  |  |
| --- | --- | --- | --- |
| **Symptoms** | **Month 12 Subjects (N=76),****n (%)** | **Month 24 Subjects (N=76),****n (%)** | **Month 36 Subjects (N=58), n (%)** |
| Any new GNE myopathy symptoms, complications or conditions? | 73 (96.1) | 71 (93.4) | 52 (89.7) |
| Tripping/foot-drop/toe-drop  | 1 (1.3) | 0 | 1 (1.7) |
| Walking funny/unsteady gait/difficulty walking  | 1 (1.3) | 1 (1.3) | 1 (1.7) |
| Frequent falls  | 4 (5.3) | 1 (1.3) | 0 |
| Weakness in legs/feet  | 3 (3.9) | 0 | 1 (1.7) |
| Weakness in arms/hands  | 0 | 1 (1.3) | 1 (1.7) |
| Fatigue  | 3 (3.9) | 2 (2.6) | 1 (1.7) |
| Muscle twitching/spasms  | 2 (2.6) | 3 (3.9) | 0 |
| Muscle pain  | 3 (3.9) | 1 (1.3) | 1 (1.7) |
| Difficulty climbing stairs  | 1 (1.3) | 0 | 1 (1.7) |
| Difficulty moving and changing positions | 5 (6.6) | 3 (3.9) | 2 (3.4) |
| Other | 1 (1.3) | 0 | 1 (1.7) |

The proportion of subjects experiencing a symptom is based on the number of subjects remaining in the study at that visit (76 for month 12 and 24, and 58 for month 36), and not the total number of subjects that enrolled (101).

**Supplemental Table 4. Summary of On-Study Adverse Events**

|  |  |
| --- | --- |
|  | **All Subjects(N=101)** |
| Subjects with an AE, n (%) |  |
|  Grade 1 | 9 (9) |
|  Grade 2 | 0 |
|  Grade 3 | 0 |
|  Grade 4 | 0 |
|  Grade 5 | 0 |
| Adverse events by preferred term, n (%) |  |
|  Back pain | 3 (3) |
|  Fatigue | 3 (3) |
|  Pain in extremity | 3 (3) |
|  Abdominal pain | 1 (1) |
|  Fall | 1 (1) |
|  Muscle spasm | 1 (1) |
|  Myalgia | 1 (1) |
|  Scar pain | 1 (1) |

AE, adverse event.