**SUPPLEMENTARY MATERIALS**

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Supplementary Table 2 Ambulatory status, Pompe Motor Function Levels, and GMFM-88 total percent scores and Week 52 changes in ADVANCE participants with IOPD who were CRIM-negative (n=14)

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Supplementary Table 4 Individual GMFM-88 items frequently improved in subgroups defined by age or disease state (≥50% or, if no items attained 50%, ≥20% of the participants in a group) within ADVANCE

Supplementary Figure 1 Patterns of GMFM-88 change from enrollment to Week 52 by Pompe Motor Function Level and motor decline status at baseline

Supplementary Table 1

ADVANCE investigators, centers, and institutional review boards (IRBs) or institutional ethics committees (IECs)

| **Investigator** | **Study site** | **Ethics approver** |
| --- | --- | --- |
| Kyrieckos A. Aleck | Phoenix Children’s Hospital, Phoenix, AZ | Phoenix Children’s Hospital IRB, Phoenix, AZ |
| Osama F. Almadhoun | University of Kansas Medical Center, Kansas City, KS | The University of Kansas Medical Center IRB, Kansas City, KS |
| Omar Abdul-Rahman | University of Mississippi Medical Center, Jackson, MS | University of Mississippi Medical Center IRB, Jackson, MS |
| Bruce A. Barshop | University of California, San Diego, CA | University of California, San Diego Human Research Protections Program, San Diego, CA |
| Jonathan Bernstein | Children's Specialty Center of Nevada, Las Vegas, NM | Western Institutional Review Board, Puyallup, WA |
| Ellen Boyd | Mission Health, Asheville, NC | Mission Health IRB, Asheville, NC |
| Barbara K. Burton | Ann & Robert Lurie Children's Hospital, Chicago, IL | Children’s Memorial Hospital IRB, Chicago, IL |
| Barry J. Byrne | University of Florida, Gainesville, FL | Western Institutional Review Board, Puyallup, WA |
| Fong Chin-To | University of Rochester Medical Center, Rochester, NY | Western Institutional Review Board, Puyallup, WA |
| Anne M. Connolly | Washington University in St. Louis, MO | Washington University in St. Louis IRB, St. Louis, MO |
| John W. Day | Stanford University, Palo Alto, CA | Stanford University Compliance Office, Palo Alto, CA |
| Debra-Lynn Day-Salvatore | St. Peter's U. Hospital, New Brunswick, NJ | Western Institutional Review Board, Puyallup, WA |
| David S. Dickens | Helen DeVos Children's Hospital Grand Rapids, MI | Spectrum Health Human IRB, Grand Rapids, MI |
| David Dimmock | Children’s Hospital of Wisconsin, Milwaukee, WI | Children’s Hospital of Wisconsin IRB, Milwaukee, WI |
| Areeg H. El-Gharbawy | Children's Hospital of Pittsburgh, PA | Western Institutional Review Board, Puyallup, WA |
| Michael J. Gambello | Emory University, Atlanta, GA | Emory University IRB, Atlanta, GA |
| James B. Gibson | ‘Specially for Children / Dell Children's Medical Group, Austin, TX | Western Institutional Review Board, Puyallup, WA |
| Kara M. Goodin | University of Louisville, KY | University of Louisville IRB, Louisville, KY |
| Christopher B. Griffith | Riley Hospital for Children, Indianapolis, IN | Indiana University IRB, Indianapolis, IN |
| Si Houn Hahn | Seattle Children’s Hospital, Seattle, WA | Seattle Children’s Hospital IRB, Seattle, WA |
| Paul R. Harmatz | Children’s Hospital and Research Center, Oakland, CA | Children’s Hospital and Research Center IRB, Oakland, CA |
| Bryce A. Heese | Children’s Mercy Hospital, Kansas City, MO | Children’s Mercy Hospital Pediatric IRB, Kansas City, MO |
| Richard E. Hillman | U. of Missouri Health Care, Columbia, MO | University of Missouri-Columbia Health Sciences IRB, Columbia, MO |
| Marybeth Hummel | Robert C. Byrd Health Science Center, Morgantown, WV | West Virginia University IRB For Protection of Human Subjects, Morgantown, WV |
| Parul Jayakar | Miami Children's Hospital, Miami, FL | Western Institutional Review Board, Puyallup, WA |
| Reena Jethva | Drexel Med St. Christopher's Hospital for Children, Philadelphia, PA | Drexel University College of Medicine Office of Regulatory Compliance, Philadelphia, PA |
| Stephen G. Kahler | Arkansas Children's Hospital, Little Rock, AR | Western Institutional Review Board, Puyallup, WA |
| Paige B. Kaplan | Children’s Hospital of Philadelphia, PA | The Children’s Hospital of Philadelphia IRB, Philadelphia, PA (initial); Western Institutional Review Board, Puyallup, WA (continued) |
| Ernest A. Kiel | Louisiana State University Health Sciences Center, Shreveport, LA | Louisiana State University IRB, Shreveport, LA |
| Joyce A. Kobori | Kaiser Permanente Northern California, Oakland, CA | Kaiser Permanente Northern California IRB, Oakland, CA |
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| Christopher M. Makris | Children's Hospital of Alabama, Birmingham, AL | Western Institutional Review Board, Puyallup, WA |
| Warren A. Marks | Cook Children’s Medical Center, Fort Worth, TX | Cook Children’s Health Care System IRB, Fort Worth, TX |
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| Mary J. Nevins | Adirondack Pediatrics, Glens Falls, NY | Glens Falls Hospital IRB, Glens Falls, NY |
| Joan E. Pellegrino | SUNY Upstate Medical University, Syracuse, NY | SUNY Upstate Medical University IRB, Syracuse, NY |
| John A. Phillips III | Vanderbilt University, Nashville, TN | Vanderbilt HRPP, Nashville, TN |
| Eniko K. Pivnick | LeBonheur Children's Hospital, Memphis, TN | University of Tennessee IRB, Memphis, TN |
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| William B. Rizzo | University of Nebraska Medical Center, Omaha, NE | University of Nebraska Medical Center IRB, Omaha, NE |
| Leslie B. Smoot | Children’s Hospital of Boston, MA | Children’s Hospital of Boston Office of Clinical Investigations, Boston, MA |
| David W. Stockton | Children's Hospital of Michigan, Detroit, MI | Wayne State University IRB, Detroit, MI |
| Duane W. Superneau | Our Lady of The Lake Regional Medical Center, Baton Rouge, LA | Western Institutional Review Board, Puyallup, WA |
| Pranoot Tanpaiboon | Children’s National Hospital, Washington, DC | Western Institutional Review Board, Puyallup, WA |
| Janet A. Thomas | Children’s Hospital of Colorado, Highlands Ranch, CO | Western Institutional Review Board, Puyallup, WA |
| David H. Viskochil | University of Utah, Salt Lake City, UT | University of Utah IRB, Salt Lake City, UT |
| Raymond Y. Wang | Children’s Hospital of Orange County, CA | Children’s Hospital of Orange County IRB |

Supplementary Table 2

Ambulatory status, Pompe Motor Function Levels, and GMFM-88 total percent scores and Week 52 changes in ADVANCE participants with IOPD who were CRIM-negative (n=14)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Genotype** | **Age group, years** | **Motor status at baseline** | **Pompe Motor Function Level** | **Pre-study motor decline?** | **Immuno-modulation?** | **Antibody titers (first, peak, Week 52)** | **Baseline GMFM-88 total % score** | **GMFM-88 change in total % score, Week 52 (percentage points)** |
| c.525delT / c.2560C>T | ≥2 | Ambulatory | II (supported walker) | No | Yes (history) | NA | 89.8 | +5.5 |
| c.525delT / c.2560C>T | <2 | Never-ambulatory | V (restricted antigravity movement) | No | Unknown | <100, 400, 200 | 15.8 | −2.5 |
| c.546+2­\_+5delTGGG / c.1650dupG | ≥2 | Ambulatory | I (walker) | No | Unknown | <100, 200, NA | 91.5 | +5.5 |
| c.546+2­\_+5delTGGG / c.1650dupG | ≥2 | Ambulatory with brace | I (walker) | No | Unknown | 3200, 6400, 3200 | 91.4 | +0.2 |
| c.1195-18\_2190\_20del / c.1195-18\_2190\_20del\* | ≥2 | Never-ambulatory; wheelchair use | V (restricted antigravity movement) | Yes | Yes (history) | 12,800, 51,200, 12,800 | 4.7 | −2.3 |
| c.1292\_1295dupTGCA / c.2560C>T | <2 | Never-ambulatory | IV (sitter) | No | Yes | 1600, 12,800, 3200 | 19.2 | +25.8 |
| c.1396delG / c.1705dupT | ≥2 | Never-ambulatory; wheelchair use | IV (sitter) | No | Yes | NA | 21.7 | −2.4  (Week 26) |
| c.1650dupG / c.2560C>T | ≥2 | Previously ambulatory; non-ambulatory at baseline | IV (sitter) | Yes | Unknown | 25,600, 102,400, 51,200 | 19.8 | −14.4 |
| c.1654delC / c.2560C>T\* | ≥2 | Previously ambulatory; non-ambulatory at baseline (wheelchair and stander use) | V (restricted antigravity movement) | No | Yes | 3200, 6400, 3200 | 9 | −3.1 |
| c.2237G>A / c.1128\_1129delinsC | ≥2 | Ambulatory | I (walker) | No | Yes | NA | 87.9 | +7.4 |
| c.2560C>T / c.2560C>T\*† | <2 | Ambulatory with foot brace and hand support | Missing data | Missing data | Yes | 3200, 6400, 3200 | Missing data | Missing data |
| c.2560C>T / c.2560C>T | ≥2 | Never-ambulatory; wheelchair use | III (supported stander) | No | Yes | NA | 58.3 | −13.8 |
| c.2560C>T / c.2560C>T | <2 | Ambulatory | I (walker) | No | Unknown | <100, 200, NA | 54.9 | +25.6 |
| c.2608C>T / c.2608C>T | <2 | Ambulatory | I (walker) | Yes | Unknown | NA | 48.1 | +9 |

CRIM, cross-reactive immunologic material; GMFM-88, Gross Motor Function Measure-88; IOPD, infantile-onset Pompe disease; NA, not available.

\*These 2 participants received 160L alglucosidase alfa temporarily and then resumed 4000L alglucosidase alfa.

†Participant died on Day 371 [after withdrawing from the study]. No Week 26 or 52 motor data are available.

Supplementary Table 3

GMFM-88 total percent scores through time in the motor analysis set (N = 90) stratified by age groups and median fraction of life on 160L alglucosidase alfa (fraction of life; overall median 0.79 derived from the full analysis set [N = 113])

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **GMFM-88 % Score** | | | | | |
| **Fraction of life < 0.79** | | | **Fraction of life ≥ 0.79** | | |
| **Baseline** | **Week 26** | **Week 52** | **Baseline** | **Week 26** | **Week 52** |
| **Overall** | | | | | | |
| N | 51 | 50 | 41 | 57 | 52 | 49 |
| Mean ± SD | 46.2 ± 33.3 | 51.2 ± 34.8 | 55.8 ± 35.6 | 46.4 ± 32.9 | 49.0 ± 35.1 | 46.6 ± 36.1 |
| Median | 47.1 | 53.3 | 63.4 | 48.1 | 56.7 | 45.6 |
| **Age at enrollment < 2 years** | | | | | | |
| N | 18 | 17 | 11 | 12 | 11 | 8 |
| Mean ± SD | 35.3 ± 23.5 | 48.1 ± 27.2 | 63.7 ± 24.4 | 41.1 ± 20.2 | 59.0 ± 21.8 | 53.9 ± 25.2 |
| Median | 29.7 | 52.6 | 63.4 | 41.1 | 64.9 | 53.7 |
| **Age at enrollment 2 to < 5 years** | | | | | | |
| N | 13 | 13 | 11 | 23 | 20 | 19 |
| Mean ± SD | 59.3 ± 29.1 | 62.0 ± 31.3 | 62.0 ± 33.4 | 45.7 ± 36.9 | 45.8 ± 42.2 | 45.6 ± 43.4 |
| Median | 64.0 | 77.8 | 84.9 | 53.1 | 38.2 | 20.6 |
| **Age at enrollment 5 to < 8 years** | | | | | | |
| N | 12 | 12 | 12 | 13 | 12 | 13 |
| Mean ± SD | 50.6 ± 40.8 | 50.2 ± 43.4 | 49.0 ± 43.2 | 46.6 ± 36.4 | 42.3 ± 35.2 | 44.1 ± 36.4 |
| Median | 48.7 | 42.8 | 34.0 | 41.9 | 43.5 | 43.0 |
| **Age at enrollment 8 to < 12 years** | | | | | | |
| N | 3 | 3 | 2 | 8 | 8 | 8 |
| Mean ± SD | 59.6 ± 49.4 | 57.2 ± 46.6 | 81.8 ± 4.6 | 51.8 ± 35.0 | 50.2 ± 34.3 | 43.4 ± 32.7 |
| Median | 78.8 | 77.8 | 81.8 | 58.0 | 56.7 | 48.2 |
| **Age at enrollment ≥ 12 years** | | | | | | |
| N | 5 | 5 | 5 | 1 | 1 | 1 |
| Mean ± SD | 32.8 ± 42.0 | 32.6 ± 41.9 | 30.8 ± 41.7 | 79.3 ± NE | 74.9 ± NE | 63.1 ± NE |
| Median | 14.3 | 15.0 | 15.5 | 79.3 | 74.9 | 63.1 |

GMFM-88, Gross Motor Function Measure-88; NE, not evaluable; SD. standard deviation.

Supplementary Table 4

Individual GMFM-88 items frequently improved in subgroups defined by age or disease state (≥50% or, if no items attained 50%, ≥20% of the participants in a group) within ADVANCE

|  |  |  |
| --- | --- | --- |
| **GMFM-88 Dimension** | **Item Description (starting position in small caps)** | **Participants improved at Week 52, n/n, (%)** |
| **Younger cohort (< 2 years of age, irrespective of disease state), n=19** | | |
| A (Lying/Rolling) | prone on forearms: Weight on R forearm, fully extends opposite arm forward | 10/19 (52.6) |
| B (Sitting) | on the floor: Attains sit on large bench | 14/19 (73.7) |
| B (Sitting) | on the floor: Attains sit on small bench | 12/19 (63.2) |
| B (Sitting) | standing: Attains sit on small bench | 10/19 (52.6) |
| C (Crawling/Kneeling) | quadruped: Crawls backwards down 4 steps on hands and knees/feet | 11/19 (57.9) |
| C (Crawling/Kneeling) | quadruped: Reaches forward with L arm, hand above shoulder level | 10/19 (52.6) |
| D (Standing) | standing: Attains squat, arms free | 10/19 (52.6) |
| D (Standing) | standing: Holding on to large bench with one hand, lifts L foot, 3 seconds | 12/19 (63.2) |
| D (Standing) | standing: Holding on to large bench with one hand, lifts R foot, 3 seconds | 12/19 (63.2) |
| D (Standing) | standing: Maintains, arms free, 3 seconds | 10/19 (52.6) |
| D (Standing) | standing: Picks up object from floor, arms free, returns to stand | 12/19 (63.2) |
| E (Walking/Running/Jumping) | standing: 1 hand held: Walks forward 10 steps | 10/19 (52.6) |
| E (Walking/Running/Jumping) | standing: Walks forward 10 steps, stops, turns 180 degrees, returns | 10/19 (52.6) |
| **Older cohort (≥ 2 years of age irrespective of disease state), n=71** | | |
| D (Standing) | standing: Lifts L foot, arms free, 10 seconds | (15/71 (21.1) |
| **IOPD group irrespective of age, n=70** | | |
| B (Sitting) | on the floor: Attains sit on large bench | 15/70 (21.4) |
| C (Crawling/Kneeling) | quadruped: Crawls backwards down 4 steps on hands and knees/feet | 14/70 (20.0) |
| C (Crawling/Kneeling) | sit on mat: Attains high kneeling position using arms, maintains, arms free, 10 seconds | 15/70 (21.4) |
| D (Standing) | standing: Attains squat, arms free | 14/70 (20.0) |
| D (Standing) | standing: Holding on to large bench with one hand, lifts L foot, 3 seconds | 15/70 (21.4) |
| D (Standing) | standing: Holding on to large bench with one hand, lifts R foot, 3 seconds | 15/70 (21.4) |
| D (Standing) | standing: Lifts L foot, arms free, 10 seconds | 16/70 (22.9) |
| D (Standing) | standing: Picks up object from floor, arms free, returns to stand | 14/70 (20.0) |
| E (Walking/Running/Jumping) | standing, holding 1 rail: Walks down 4 steps, holding 1 rail, alternating feet | 16/70 (22.9) |
| E (Walking/Running/Jumping) | standing, holding 1 rail: Walks up 4 steps, holding 1 rail, alternating feet | 17/70 (24.3) |
| **LOPD group irrespective of age, (n=20)** | | |
| A (Lying/Rolling) | supine: Flexes L hip and knee through full range | 4/20 (20.0) |
| A (Lying/Rolling) | supine: Lifts head 45 degrees | 4/20 (20.0) |
| B (Sitting) | supine: hands grasped by examiner: Pulls self to sitting with head control | 4/20 (20.0) |
| C (Crawling/Kneeling) | high kneel: Knee-walks forward 10 “steps”, arms free | 4/20 (20.0) |
| C (Crawling/Kneeling) | sitting on mat: Attains high kneel using arms, maintains, arms free, 10 seconds | 4/20 (20.0) |
| D (Standing) | standing: Holding on to large bench with one hand, lifts L foot, 3 seconds | 4/20 (20.0) |
| D (Standing) | standing: Holding on to large bench with one hand, lifts R foot, 3 seconds | 5/20 (25.0) |
| D (Standing) | standing: Lifts L foot, arms free, 10 seconds | 7/20 (35.0) |
| D (Standing) | standing: Lifts R foot, arms free, 10 seconds | 9/20 (45.0) |
| D (Standing) | standing: Lowers to sit on floor with control, arms free | 4/20 (20.0) |
| D (Standing) | standing: Picks up object from floor, arms free, returns to stand | 5/20 (25.0) |
| E (Walking/Running/Jumping) | standing, holding 1 rail: Walks down 4 steps, holding 1 rail, alternating feet | 4/20 (20.0) |
| E (Walking/Running/Jumping) | standing, holding 1 rail: Walks up 4 steps, holding 1 rail, alternating feet | 4/20 (20.0) |
| E (Walking/Running/Jumping) | standing: Jumps forward 30 cm (12") high, both feet simultaneously | 4/20 (20.0) |
| E (Walking/Running/Jumping) | standing: Runs 4.5m (15'), stops and returns | 4/20 (20.0) |
| E (Walking/Running/Jumping) | standing: Walks down 4 steps, alternating feet | 5/20 (25.0) |

GMFM, Gross Motor Function Measure; IOPD, infantile-onset Pompe disease; L, left; LOPD, late-onset Pompe disease; R, right.

Supplementary Figure 1

Patterns of GMFM-88 change from enrollment to Week 52 by Pompe Motor Function Level and motor decline status at baseline

Chart

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