Digital Biomarkers

Digit Biomark , DOI: 10.1159/000550259
Received: June 26, 2025
Accepted: December 19, 2025
Published online: January 6, 2026

Actigraphy-Quantified Physical Activity Measurements in Patients With Symptomatic LMNA-Related Dilated Cardiomyopathy in REALM-DCM

Garcia-Pavia P, Cai X, Di J, Li H, Demanuele C, Bruno J, Hinnershitz TM, Angeli FS, MacRae CA

ISSN: (Print), eISSN: 2504-110X (Online)
https://www.karger.com/DIB
Digital Biomarkers

Brief Report

Actigraphy-Quantified Physical Activity Measurements in Patients With Symptomatic *LMNA*-Related Dilated Cardiomyopathy in REALM-DCM

Pablo Garcia-Pavia, MD, PhD[1,*] Xuemei Cai, MD[2,*] Junrui Di, PhD[3] Huihua Li, MS[3] Charmaine Demanuele, PhD[3] Jonathan Bruno, MBA[2] Tina Marie Hinnershitz, BSc[4] Franca S. Angeli, MD, PhD[3] and Calum A. MacRae, MD, PhD[5]
*Co-first authors.
[1]Hospital Universitario Puerta de Hierro Majadahonda, CIBERCV, IDIPHISA, and Centro Nacional de Investigaciones Cardiovasculares, Madrid, Spain
[2]Pfizer Inc, Cambridge, (MA,) USA
[3]Pfizer Inc, New York, (NY,) USA
[4]Pfizer Inc, Collegeville, (PA,) USA
[5]Cardiovascular Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, (MA,) USA

Short title: REALM-DCM: Actigraphy-Quantified PA

Corresponding author: Xuemei Cai, MD
Address: Pfizer, Inc
Cambridge, MA 02139
Email: Xuemei.Cai@pfizer.com
Telephone: (617) 335 - 9260

Keywords: Wearable physical activity monitoring, Heart failure, Dilated Cardiomyopathy, Digital Biomarkers, Clinical Study

Abstract

Introduction:

Actigraphy-quantified physical activity (PA) allows for continuous measurements of physical activity that are reflective of real-world day-to-day functioning and morbidity in persons living with cardiomyopathy. This analysis reports the results of actigraphy monitoring and relates these to other clinical outcome assessments in the Phase 3, multinational REALM-DCM (NCT03439514) clinical trial in *LMNA*-related dilated cardiomyopathy.

Methods:

Between 2020 and 2022, REALM-DCM randomized 37 patients with actigraphy worn on the non-dominant wrist continuously to monitor daily physical activity. Of those 35 participants had analyzable data for this analysis.

Results:

The median duration of actigraphy monitoring for all participants was 293 days across 120 patient visits. Over 85% of the visits met a predefined threshold of wear-time compliance of ten hours of awake wear time for at least four days within the two-week monitoring period prior to and after clinic visits. Kansas City Cardiomyopathy Questionnaire (KCCQ) physical limitation scores was positively associated with several actigraphy-quantified PA metrics, including Moderate to Vigorous Physical Activity (MVPA), moderate activity, non-sedentary behavior, total step counts, total activity counts (all 3 axes and their vector magnitude). 6 minute walk time (6MWT) distance was positively associated with time spent in MVPA and moderate activity, and total step counts. Patient Global Impression (PGI) Symptom Heart Failure Severity were negatively associated with non-sedentary behavior, total activity counts (vector magnitude, X, and Y axes), and light activity. Actigraphy endpoints also distinguished between NYHA class II and class III patients. Actigraphy endpoints did not correlate with the KCCQ total score.

Conclusion:

This is the largest and most longitudinal dataset of LMNA-DCM patients collected and reported to date using wearable sensors to gain understanding of physical activity patterns in these patients. These data help to understand the potential use of actigraphy monitoring and wearable technologies in genetic cardiomyopathy and heart failure clinical trials.

Introduction

Lamin A/C gene (*LMNA)*–related dilated cardiomyopathy (DCM) is a rare autosomal dominant disease characterized by chronic heart failure (CHF), conduction disorders, and life-threatening arrhythmias [1]. Despite guideline-recommended therapies, patients with *LMNA*-related DCM usually progress, highlighting an unmet treatment need [1].

In 2019, the US Food and Drug Administration released the draft guidance "Treatment for Heart Failure: Endpoints for Drug Development," suggesting patients' subjective symptoms and function (eg, measures of daily activity) as potential efficacy endpoints in clinical trials [2][3]. Limitations in physical activity (PA) are features of HF associated with poor prognosis [3]. Digital health technologies (DHTs; eg, accelerometry, actigraphy) can provide granular and real-time insights on patient functioning across multiple dimensions [4]. Actigraphy is a non-invasive and objective method of assessing PA by monitoring movements using sensors and accompanying algorithms. Although trials incorporating actigraphy-quantified PA (AQPA) outcomes have increased in recent years, studies on patients with genetic cardiomyopathies, standardization of device and analytical approach, and validated endpoints and patient populations are lacking.

This paper assessed associations between AQPA metrics and clinical endpoints using data from the randomized, double-blind, placebo-controlled, phase 3 REALM-DCM trial (NCT03439514), investigating efficacy and safety of ARRY-371797 in patients with symptomatic *LMNA*-related DCM [1]. Compliance, data completeness and the association between actigraphy measured PA metrics with other clinical points including 6MWT, KCCQ, and N-terminal prohormone of brain natriuretic peptide (NTproBNP) is examined.

Methods

The REALM-DCM trial design, ethics statement, and outcomes have been previously published [1]. Actigraphy was added as an exploratory endpoint after a protocol amendment (February 2021). REALM-DCM was terminated early after a planned interim analysis suggested futility [1].

Patients continuously wore the E.200.4004 ActiGraph CentrePoint Insight Watch (ActiGraph, Pensacola, Florida; https://theactigraph.com/cpiw) on their non-dominant wrist deploying firmware E.208. Real-time data collection (sample rate: 64 Hz), monitoring, and automated alerts about device malfunction and non-compliance were performed through device-to-cloud data transfer.

AQPA metrics included time spent for light, moderate, moderate-to-vigorous, and vigorous activity; non-sedentary and sedentary behavior; total step counts; total activity counts (combined or individual x-, y-, z-axis); mean activity count/hr during the most active 10 hours (M10hr), 1 hour (M60min), 15 minutes (M15min), and 6 minutes (M6min) of the day; and mean activity count/hr for the least active 5 hours of the day (L5hr). Data were derived using algorithms in the ActiGraph CentrePoint Version 3 API (https://github.com/actigraph/CentrePoint3APIDocumentation) [5]. AQPA assessments were performed throughout the study (baseline, weeks 4, 12, and every 12 weeks thereafter), reflecting patient follow-up visits for clinical assessments. Daily AQPA measurements were considered valid with ≥10 hours of awake wear time. During each assessment period, the 14-day analytical window of interest included 7 days before and 7 days after clinic visit, excluding the day of visit as non-representative of patients' daily routine. Patients with ≥4 days of valid AQPA measurements within the 14-day period were considered compliant and included in the analysis.

Associations between each clinical outcome (six-minute walk test [6MWT] distance, Kansas City Cardiomyopathy Questionnaire physical limitation/total symptom scores [KCCQ-PLS/-TSS], N-terminal pro–B-type natriuretic peptide [NT-proBNP] concentration, and Patient Global Impression of Severity-PA limitation/Severity of HF symptom [PGIS-PAL/-SHFS] score) and AQPA metric were evaluated using a mixed effects model. Each AQPA metric was considered the response and each clinical outcome as fixed effect, and a random patient intercept. Standardized coefficients from the mixed effects models for the clinical outcome will be reported to represent the magnitude and direction of the linear association, Differences between subgroups based on age (18–49, 50–64, ≥65 years) and New York Heart Association (NYHA) class (II, III) were assessed using a mixed effects model with both age groups and NYHA class as the fixed effects, and a random patient intercept. For

significant between group differences, Cohen's effect sizes will be reported. Analyses were conducted using R 4.2.2 (R Foundation, Vienna, Austria).

Results

In REALM-DCM, 77 patients received ARRY-371797 (n = 40) or placebo (n = 37) (shown in **Fig. 1**) [1]. From February 2021 to October 2022, 35 of 37 patients who consented to actigraphy had evaluable data and contributed to a combined total of 120 patient visits. Patients (mean age, 53 years) were mostly male (60%) and white (97%) with NYHA class II HF (86%) (shown in **Table 1**).

Across all patient visits, 85% had ≥4 days of valid AQPA data and on average (mean [standard deviation, SD]), 7.9 (4.46) compliant days/visit. The median duration for actigraphy monitoring was 293 days. On average (mean [SD]), patients wore the device for 18.63 (7.08) hr/day and 11.42 (4.35) awake hr/day.

Among clinical outcomes, KCCQ-PLS was positively associated with many AQPA metrics, including moderate-to-vigorous PA (MVPA), moderate activity, non-sedentary behavior, and total step and activity counts (shown in **Fig. 2A** in terms of the standardized coefficients for the clinical outcomes from the mixed effects model). 6MWT was positively associated with MVPA, moderate activity, and total step counts. PGIS-SHFS was negatively associated with non-sedentary behavior, total activity counts, and light activity, whereas NT-proBNP was negatively associated with L5hr. KCCQ-TSS and PGIS-PAL were not associated with any AQPA metric.

Least squares means for several AQPA metrics were significantly different between patients with NYHA class II vs III HF (shown in **Fig. 2B**) and Cohen's effect sizes were estimated to be ranged from 1.84 to 2.68 which were considered large (Supplementary Table 2). AQPA metrics were not statistically different between age groups.

Discussion

This analysis, to our knowledge, provides the first data using actigraphy to measure PA in patients with genetic cardiomyopathies (eg, *LMNA*-related DCM). The findings are broadly similar to studies in patients with generic HF [4][6][7][8]. KCCQ-PLS and 6MWT were positively associated with several AQPA metrics, including time spent in moderate and moderate-to-vigorous activity, non-sedentary behavior, and total step or activity counts, whereas KCCQ-TSS was not associated with any metric. NT-proBNP was negatively associated with L5hr. PGIS-SHFS was negatively associated with non-sedentary behavior, total activity counts, and light activity, whereas PGIS-PAL was not associated with any metric. These data suggest that individual AQPA metrics may not fully capture the granularity of meaningful PA and therefore may incompletely represent subjective clinical symptoms in patients with *LMNA*-related DCM or HF. Nevertheless, decreased AQPA distinguished patients with NYHA class III vs II HF. Additional work is necessary to derive rigorous objective metrics on the range of daily PAs integrated in subjective symptom scores for disorders with varying neuromuscular and metabolic effects.

Although only 35 patients had AQPA data in REALM-DCM, the median duration of PA monitoring was considerably longer than that of earlier studies (42 vs 12 weeks) [6][8]. In the CHIEF-HF trial, results from patients wearing Fitbit Versa 2 showed association between increasing 25-point ranges of KCCQ-PLS/-TSS had progressively higher daily step counts and greater number of mean floors climbed up to an inflection point of approximately 2000 steps [6]. In our analysis of the LMNA-DCM population in REALM-DCM, the total step count was also positively correlated with KCCQ-PLS as were most of the PA measures assessed including MVPA, moderate activity, non-sedentary behavior, and total activity counts (all 3 axes and vector magnitude). 6MWD was also positively associated with time spent in MVPA, moderate activity, and total step count. Interestingly, M6min which is the mean activity level during the maximum daily 6 minutes of activity was not correlated with the 6MWD in this patient population. Previously, a study in elderly HF patients (³65 years of age) has shown a correlation between the maximum six minutes of daily activity with 6MWD although that correlation was lower in younger (<65 years of age) HF patients [4].

In 2021, the OUTSTEP-HF trial reported 6MWT distance improved (35.09m) after 12 weeks of sacubitril/valsartan vs enalapril treatment, without improvements in average daytime non-sedentary activity and M6min [8]. In the mixed effects model for the REALM-DCM trial, there was no correlation between daily non-sedentary activity and 6MWT although there was a positive correlation with daily non-sedentary activity and KCCQ-PL. Further longitudinal studies will be needed to better understand the reproducibility and clinical meaning of actigraphy-quantified PA measures over time and further understanding of which of these measures are clinically meaningful and by what degree.

This exploratory analysis has several limitations. REALM-DCM was not powered to analyze actigraphy data and excluded patients with impaired ability to perform the 6MWT. Therefore, findings may not represent the general population with *LMNA*-related DCM and must be interpreted with caution. Some AQPA metrics and algorithms were developed in healthy individuals and require independent validation in patients with HF, which has well-known effects on multiple physiologic systems. Moreover, some of the algorithms deployed in this study were previously validated in healthy individuals but used in this study for a HF population. Dibben et al, 2020 previously have shown that patients with HF may expend more energy as measured by metabolic equivalents (METs and VO_2) to accomplish the same activity as a healthy volunteer [9]. To potentially overcome this limitation, other measures that are agnostic to normative values were used including total activity counts and mean activity levels. Despite these limitations, to our knowledge, this analysis presents the largest AQPA data set for patients with *LMNA*-related DCM and the longest overall duration for DHT monitoring in a phase 3 study of CHF.

Actigraphy provides objective assessment of PA that could help in designing and conducting clinical trials. There is an ongoing need for therapies to treat persons living with different forms of HF including *LMNA*-related DCM and a growing trend towards obtaining continuous longitudinal data using DHTs to complement traditional episodic clinical assessments. However, further studies are needed to establish clinically relevant AQPA metrics that can detect treatment differences. While this analysis did not evaluate treatment differences, our findings support future efforts to establish the validity of AQPA as a complement or alternative to traditional clinical efficacy measures including subjective symptom scores. Combined information gathered from qualitative patient interviews and quantitative data analysis from future clinical trials where efficacy is demonstrated will help develop a range of values representing meaningful within-patient change for the AQPA endpoints and other digital metrics. Growing this body of evidence around content validity, convergent validity, predictive validity, reproducibility, and responsiveness to intervention as well as the relevant costs, will support inclusion of these novel endpoints in future trials.

Conclusions

This is the largest wearable dataset collected from LMNA-DCM patients collected and reported to date using wearable sensors to gain understanding of physical activity patterns in these patients. This dataset also describes the longest overall duration of wearable monitoring in CHF patients over the course of a Phase 3 study. NYHA classes were distinguished by all of the measures examined over time using actigraphy. Time spent in MVPA, moderate activity, and total step count were positively correlated with 6MWT and KCCQ-PL. Additionally, total activity count was positive correlated with KCCQ-PL. In contrast, only L5hr on actigraphy correlated with NT-proBNP and no actigraphy measures examined in this population that correlated with KCCQ-TS, suggesting that these wearable metrics are better correlated to physical activity limitations as captured by the KCCQ questionnaire. These data add to the growing body of work of actigraphy in HF studies and understanding the potential uses of these and many other wearable or sensing technologies in future clinical trials.

Statements

Acknowledgement (optional)

The authors thank all patients, clinical investigators, and staff who took part in REALM-DCM and Dr. Wenyi Lin for checking the quality of the statistical analyses. Medical writing support was provided by April Cabang of Engage Scientific Solutions and was funded by Pfizer.

Statement of Ethics

The REALM-DCM study protocol was approved by the independent review board or ethics committee at each participating site and was conducted in accordance with the Declaration of Helsinki and the International Conference on Harmonization–Good Clinical Practice guidelines. All patients provided written, informed consent. A listing of all sites where the study was approved by independent review board or ethics committee were previously published with the main study results in Garcia-Pavia P. *et al*, 2024 [1].

Conflict of Interest Statement

PG-P reports speaking fees from Alnylam Pharmaceuticals, AstraZeneca, BMS, BridgeBio, Intellia, Ionis Pharmaceuticals, Novo Nordisk, and Pfizer; consulting fees from Alexion, Alnylam Pharmaceuticals, AstraZeneca, Attralus, Bayer, Biomarin, Bristol Myers Squibb, BridgeBio, Cytokinetics, Daiichi Sankyo, Edgewise, General Electric, Idoven, Intellia, Ionis Pharmaceuticals, Lexeo, Neuroimmune, Novo Nordisk, Pfizer, and Rocket Pharmaceuticals; and research/educational support to his institution from Alnylam, AstraZeneca, BridgeBio, Intellia, Novo Nordisk, and Pfizer. **XC, JD, HL, CD, JB, TMH, FSA** are employees of Pfizer and hold stock and/or stock options. **CAM** reports consultancy fees from Affinia, Array BioPharma, AstraZeneca, Bayer, Bristol Myers Squibb, Design Therapeutics, Dewpoint, DiNAQOR, Merck, MyoKardia, Novartis, and Pfizer; and grant support from Bayer, Merck, Novartis, and Sanofi.

Funding Sources

This study was sponsored by Pfizer.

Author Contributions

PG-P, XC, JD, HL, CD, JB, TMH, FSA, CAM, FSA: Conceptualization and design. **PG-P, TMH, FSA, CAM:** Data collection and study execution. **JD, HL, CD:** Analysis. **XC, JD, HL, JB, FSA:** Drafting of manuscript. **PG-P, XC, JD, HL, CD, JB, TMH, FSA, CAM:** Review and revision of the manuscript. All authors had full access to the study data and approved this manuscript.

Data Availability Statement

The data that support the findings of this study are not publicly available due to privacy reasons. Upon reasonable request and subject to review, Pfizer will provide the data that support the findings of this study. Subject to certain criteria, conditions, and exceptions, Pfizer may also provide access to the related individual de-identified participant data. To make a data access request, please go to https://www.pfizer.com/science/clinical-trials/trial-data-and-results for more information.

References

1. Garcia-Pavia P, Palomares JFR, Sinagra G, et al. REALM-DCM: a phase 3, multinational, randomized, placebo-controlled trial of ARRY-371797 in patients with symptomatic LMNA-related dilated cardiomyopathy. *Circ Heart Fail*. 2024;17(7):e011548. doi:10.1161/CIRCHEARTFAILURE.123.011548
2. Treatment for heart failure: endpoints for drug development: guidance for industry. US Department of Health and Human Services. Food and Drug Administration. Center for Drug Evaluation and Research. Center for Biologics Evaluation and Research. Updated June 2019. Accessed December 2, 2024. https://www.fda.gov/media/128372/download.
3. Strath SJ, Kaminsky LA, Ainsworth BE, et al. Guide to the assessment of physical activity: clinical and research applications: a scientific statement from the American Heart Association. *Circulation*. 2013;128(20):2259-2279. doi:10.1161/01.cir.0000435708.67487.da
4. Howell J, Strong BM, Weisenberg J, et al. Maximum daily 6 minutes of activity: an index of functional capacity derived from actigraphy and its application to older adults with heart failure. *J Am Geriatr Soc*. 2010;58(5):931-936. doi:10.1111/j.1532-5415.2010.02805.x
5. Neishabouri A, Nguyen J, Samuelsson J, et al. Quantification of acceleration as activity counts in ActiGraph wearable. *Sci Rep*. 2022;12(1):11958. doi:10.1038/s41598-022-16003-x
6. Golbus JR, Gosch K, Birmingham MC, et al. Association between wearable device measured activity and patient-reported outcomes for heart failure. *JACC Heart Fail*. 2023;11(11):1521-1530. doi:10.1016/j.jchf.2023.05.033
7. Izawa KP, Kasahara Y, Watanabe S, et al. Association of objectively measured daily physical activity and health utility to disease severity in chronic heart failure patients: A cross-sectional study. *Am Heart J Plus*. 2021;10:100051. doi:10.1016/j.ahjo.2021.100051
8. Piepoli MF, Hussain RI, Comin-Colet J, et al. OUTSTEP-HF: randomised controlled trial comparing short-term effects of sacubitril/valsartan versus enalapril on daily physical activity in patients with chronic heart failure with reduced ejection fraction. *Eur J Heart Fail*. 2021;23(1):127-135. doi:10.1002/ejhf.2076
9. Dibben GO, Gandhi MM, Taylor RS, et al. Physical activity assessment by accelerometry in people with heart failure. *BMC Sports Science, Medicine, and Rehabilitation*. 2020;12:47. doi: 10.1186/s13102-020-00196-7

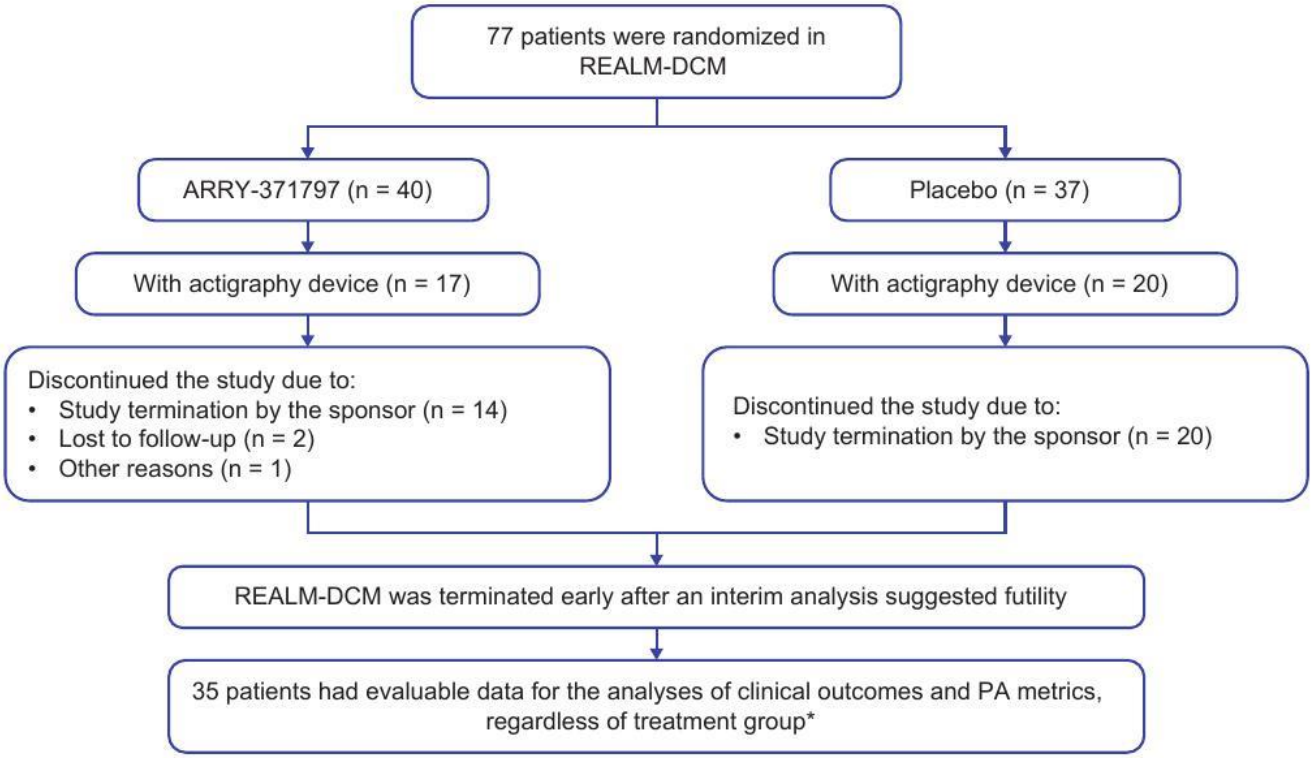
Figure Legends

Fig. 1. Patient disposition.

*****As there were no treatment differences observed in REALM-DCM, patients who received ARRY-371797 or placebo were combined in this study.[1]

Fig. 2. Standardized estimated coefficients from the mixed effects models assessing the association between AQPA and clinical measures (**A**) and estimated differences in AQPA between NYHA classes (**B**). In Fig. 2A, the T-score was used as a standardized representation to facilitate clearer visualization of the strength of the association. A positive standardized coefficient implies a positive relationship, while a negative standardized coefficient implies a negative relationship. Empty squares indicate that the association is not statistically significant ($P > 0.05$). No imputations were conducted for missing data. Total activity counts refer to the sum of daily total activity counts for all vector magnitudes (x, y, and z axes).

6MWT, six-minute walk test; AQPA, actigraphy-quantified physical activity; CI, confidence interval; KCCQ-PLS, Kansas City Cardiomyopathy Questionnaire-physical limitation score; KCCQ-TSS, Kansas City Cardiomyopathy Questionnaire-total symptom score; L5hr, least active 5 hours of the day; LS, least squares; M6min, most active 6 minutes of the day; M15min, most active 15 minutes of the day; M60min, most active 60 minutes of the day; M10hr, most active 10 hours of the day; MVPA, moderate-to-vigorous physical activity; NT-proBNP, N-terminal pro–B-type natriuretic peptide; NYHA, New York Heart Association; PA, physical activity; PAL, physical activity limitation; PGIS, Patient Global Impression of Severity; SFHS, severity of heart failure symptom.



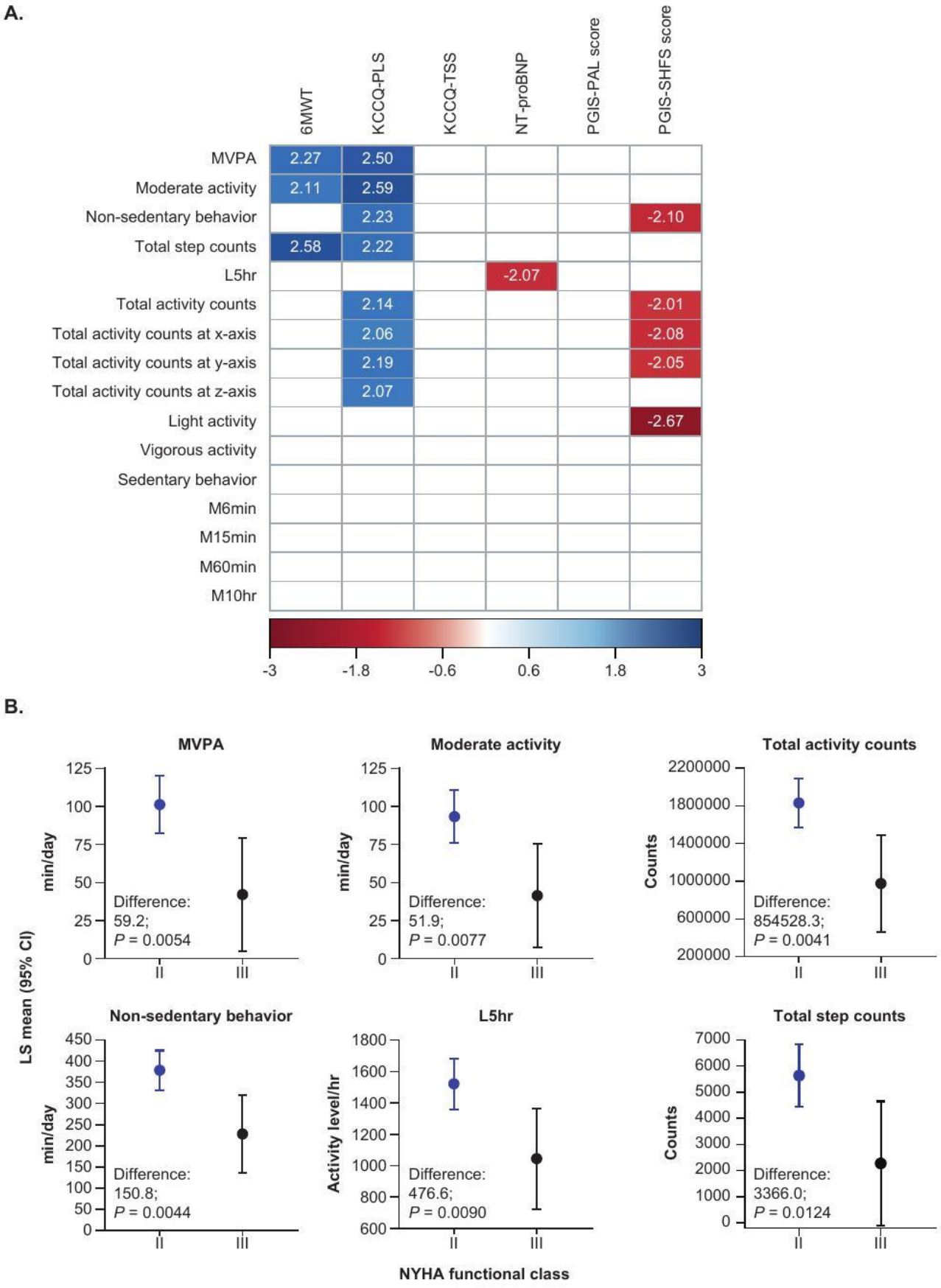


Table 1 Baseline demographics and clinical characteristics

Variable	Patients (n = 35)
Age, years	
Mean (SD)	52.97 (10.46)
Median (range)	60.00 (24.00–70.00)
Categories, n (%)	
18–49	13 (37.14%)
50–64	18 (51.43%)
≥65	4 (11.43%)
Sex, n (%)	
Male	21 (60.00%)
Female	14 (40.00%)
Treatment group, n (%)	
ARRY-371797	15 (42.86%)
Placebo	20 (57.14%)
NYHA functional class, n (%)	
II	30 (85.71%)
III	5 (14.29%)
NT-proBNP, pg/mL	
Mean (SD)	137.29 (105.96)
Median (range)	111.98 (20.06–363.44)
6MWT distance, m	
Mean (SD)	390.69 (54.41)
Median (range)	402.50 (238.47–460.25)
KCCQ-PLS	
Mean (SD)	69.48 (20.78)
Median (range)	70.83 (20.83–100.00)

KCCQ-TSS	
Mean (SD)	71.96 (16.67)
Median (range)	70.83 (35.42–100.00)
PGIS – PAL score	
Mean (SD)	1.49 (0.89)
Median (range)	2.00 (0.00–3.00)
PGIS – SHFS score	
Mean (SD)	1.40 (0.65)
Median (range)	1.00 (0.00–2.00)
PA measures*	**n = 7**
Light activity, min/day	
Mean (SD)	604.87 (257.18)
Median (range)	718.15 (186.06–845.21)
Moderate activity, min/day	
Mean (SD)	82.99 (56.23)
Median (range)	93.58 (4.19–162.04)
MVPA, min/day	
Mean (SD)	87.53 (59.35)
Median (range)	101.71 (4.19–170.00)
Vigorous activity, min/day	
Mean (SD)	4.54 (4.00)
Median (range)	4.98 (0.00–8.89)
Total activity counts	
Mean (SD)	1618044.65 (1029877.14)
Median (range)	1780759.10 (53260.28–2955624.30)
Total activity counts at x-axis	
Mean (SD)	873648.50 (535625.53)
Median (range)	993256.93 (32391.50–1501949.93)

Total activity counts at y-axis	
Mean (SD)	878722.61 (587005.37)
Median (range)	963461.04 (28366.75–1708638.00)
Total activity counts at z-axis	
Mean (SD)	1036188.76 (659876.66)
Median (range)	1115569.07 (31063.00–1883516.79)
Total step count	
Mean (SD)	4569.44 (2897.74)
Median (range)	4342.90 (269.50–8159.50)
Non-sedentary behavior, min/day	
Mean (SD)	321.79 (173.22)
Median (range)	387.96 (38.62–502.36)
Sedentary behavior, min/day	
Mean (SD)	370.61 (129.42)
Median (range)	410.85 (151.62–517.55)
M6min, activity level/day	
Mean (SD)	8559.48 (1837.86)
Median (range)	8760.39 (5968.30–10901.75)
M15min, activity level/day	
Mean (SD)	7000.84 (1614.23)
Median (range)	7293.28 (5007.16–9226.52)
M60min, activity level/day	
Mean (SD)	5190.25 (1186.56)
Median (range)	5440.83 (3775.85–6540.63)
M10hr, activity level/hr	
Mean (SD)	5248.36 (1104.23)
Median (range)	5440.83 (4066.40–6540.63)
L5hr, activity level/hr	

Mean (SD)	1500.01 (240.57)
Median (range)	1519.07 (1243.11–1737.56)

*Data 14 days before to Day -1 clinical site visit were used for baseline PA. Only 7 patients were recruited after the protocol amendment and therefore had PA measurements at baseline visits.

6MWT, six-minute walk test; KCCQ-PLS, Kansas City Cardiomyopathy Questionnaire – physical limitation score; KCCQ-TSS, Kansas City Cardiomyopathy Questionnaire – total symptom score; L5hr, least active 5 hours of the day; M6min, most active 6 minutes of the day; M15min, most active 15 minutes of the day; M60min, most active 60 minutes of the day; M10hr, most active 10 hours of the day; MVPA, moderate-to-vigorous physical activity; NT-proBNP, N-terminal pro–B-type natriuretic peptide; NYHA, New York Heart Association; PA, physical activity; PAL, physical activity limitation; PGIS, Patient Global Impression of Severity; SD, standard deviation; SHFS, severity of heart failure symptom.