#PCR230

# Patient-Reported Outcomes From a Phase 3 Study of Givinostat in Patients With Duchenne Muscular Dystrophy

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## BACKGROUND

- Patients with Duchenne muscular dystrophy (DMD) experience progressive loss of function that is associated with a substantial reduction in daily activities, which can decrease quality of life (QoL)
- Givinostat is an oral histone deacetylase inhibitor that was investigated in DMD in the randomized, double-blind, placebo-controlled, phase 3, EPIDYS trial (NCT02851797), based on its potential to slow functional decline[1]

## OBJECTIVE

- To evaluate patient-reported outcome data assessed via the Pediatric Outcome Data Collection Instrument (PODCI) from the phase 3 EPIDYS study, which compared the efficacy and safety of givinostat vs placebo in addition to the standard of care (ie, corticosteroids) in ambulant boys aged ≥6 years with DMD

## METHODS

- The PODCI has been used to evaluate activities of daily living, pain, and happiness in patients with DMD and their caregivers
- The PODCI includes 5 subscales: upper extremity function, transfer and basic mobility, sports/physical function, pain/comfort, and happiness. The global function scale is a combination of the upper extremity function, transfer and basic mobility, sports/physical function, and pain/comfort subscales
  - Scores range from 0 (poor outcome/worst health) to 100 (best outcome/best health), with higher scores indicating better QoL[2]
- Previously published data on PODCI in DMD reported baseline mean (SD) global function scores of 71.4 (12.1) in patients aged 7-10 years and 68.1 (10.9) in patients aged >10 years[3]
- In EPIDYS, PODCI questionnaires were completed by caregivers ("Parent") or by patients themselves if aged ≥10 years ("Self") at baseline and at months 12 and 18
  - Respondents may differ from baseline to post-baseline evaluations; however, post-hoc analysis determined that Parent and Self scores were considered reliable and comparable. Parent and Self evaluations were analyzed together as equivalent measures
- Least squares (LS) means, CIs, and nominal *P* values were obtained from an analysis of covariance model on change from baseline in the standardized PODCI score at month 18
  - Baseline standardized PODCI score and rederived age at first dose were fitted as covariates, with concomitant corticosteroid use and treatment group as independent classification factors

## CONCLUSIONS

- Patients treated with givinostat showed smaller reductions in activities of daily living and QoL across most PODCI subscales compared with placebo
- While the differences in QoL between the 2 groups were not statistically significant, the data suggest that givinostat may slow the decline of activities of daily living and QoL in patients with DMD relative to placebo. Additional studies may be warranted to support these findings

## RESULTS

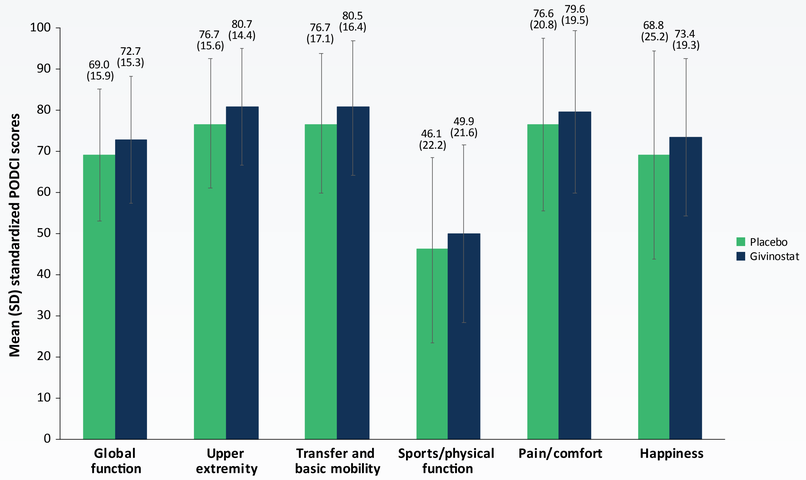
**TABLE 1. Standardized PODCI global function and subscale scores at baseline**

| PODCI | Global function | Upper extremity | Transfer and basic mobility | Sports/physical function | Pain/comfort | Happiness |
|---|---|---|---|---|---|---|
| Givinostat, mean (SD) (n=81) | 77.2 (12.5) | 82.9 (12.0) | 86.6 (12.4) | 59.7 (17.9) | 79.4 (16.7) | 76.5 (18.9) |
| Placebo, mean (SD) (n=39) | 76.9 (12.9) | 80.9 (12.7) | 86.2 (12.0) | 58.5 (22.0) | 82.1 (18.2) | 77.1 (20.9) |

Abbreviation: PODCI, Pediatric Outcome Data Collection Instrument.
Note: The global function scale includes the upper extremity function, transfer and basic mobility, sports/physical function, and pain/comfort subscales.

- These analyses included 81 patients treated with givinostat and 39 patients who received placebo in addition to standard of care
- Baseline mean (SD) PODCI global function and subscale scores for givinostat and placebo groups are listed in **Table 1**

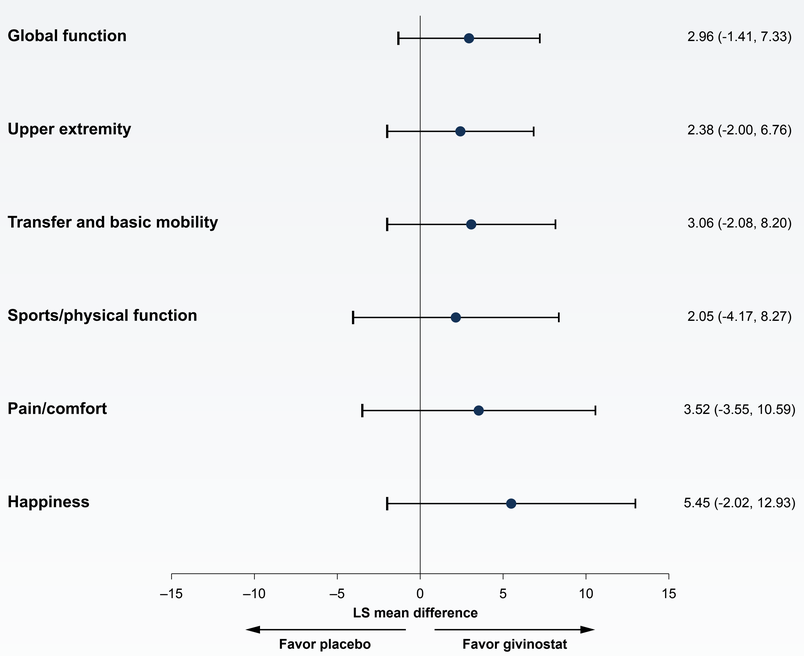
**FIGURE 1. Standardized PODCI scores at 18 months**




Abbreviation: PODCI, Pediatric Outcome Data Collection Instrument.
Note: The PODCI questionnaires were completed by either caregivers or patients; respondents may differ across visits, but were analyzed together as equivalent based on post-hoc analysis.

- At 18 months, mean (SD) subscale scores were consistently higher (not statistically significant) for givinostat than placebo across subscales (**Figure 1**)
- At 12 months, mean (SD) PODCI global function scores were 73.9 (13.4) for givinostat and 72.9 (13.6) for placebo, and at 18 months, scores were 72.7 (15.3) for givinostat and 69.0 (15.9) for placebo, indicating less functional decline for patients who received givinostat compared with placebo (not statistically significant)
  - Trends were generally similar across subscales, with givinostat-treated patients maintaining higher scores than placebo
  - However, for pain/comfort, baseline and 12-month scores were lower for givinostat, while at 18 months, scores were higher compared with placebo

**FIGURE 2. Treatment effect (givinostat – placebo) on PODCI scores: LS mean difference in change from baseline to 18 months**




Abbreviations: LS, least squares; PODCI, Pediatric Outcome Data Collection Instrument.
Note: The PODCI questionnaires were completed by either caregivers or patients; respondents may differ across visits, but were analyzed together as equivalent based on post-hoc analysis.

- Although not statistically significant, the LS mean difference (givinostat – placebo) in the PODCI global function and happiness subscore change from baseline to 18 months favored givinostat. Individual component subscores that make up the global function score showed similar results (**Figure 2**)

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**REFERENCES**
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