Modelling The Benefit of Givinostat on Duchenne Muscular Dystrophy Patients, and Their Caregivers

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INTRODUCTION

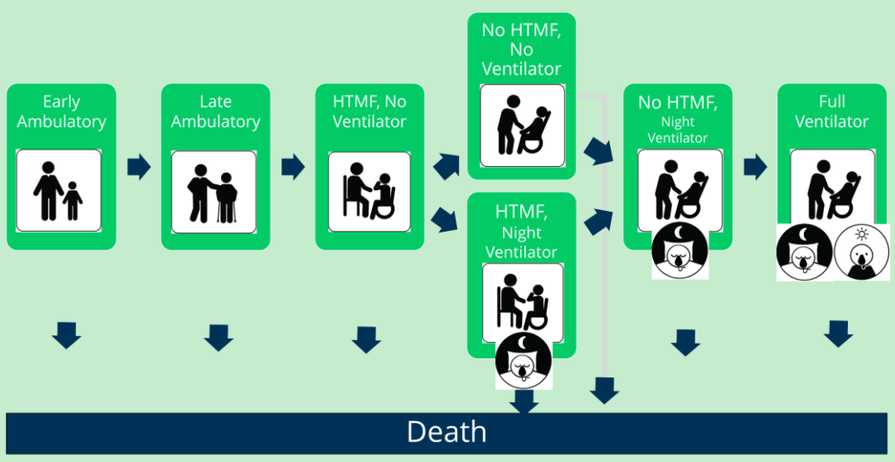
Duchenne Muscular Dystrophy (DMD) is a rare, progressive, and lethal X-linked recessive disorder, caused by mutations in the dystrophin gene[1], which primarily affects males with a prevalence of 2.8 per 100,000 in Europe[2]. DMD is characterized by early progressive muscle injury, resulting in the loss of ambulation (LOA), impaired and loss of upper limb function, wheelchair dependency and premature death due to respiratory failure or cardiac insufficiency. The decline in motor function, impacts both patient and caregiver's burden.

OBJECTIVE

- To model the benefit of givinostat on the disease progression of DMD patients estimated through the cost-effectiveness model (CEM)
- To estimate the impact of extending patients' lives in the earlier phases of the disease on both patient and caregivers

METHODS

Project Hercules' Markov model was adapted with the EPIDYS phase III trial[3] and the open label extension study of givinostat (Study-51)[4]



HTMF – Hand To Mouth Function

Figure 1. DMD Markov Model
(adapted project Hercules) *Possibility to remain or transition HS at the end of each cycle.*

- The **relative efficacy of givinostat** to estimate **Health State (HS) transitions** compared to natural history, was obtained from a propensity score matched analysis of givinostat[5] and compared versus the model comparator (corticosteroids) of the Project HERCULES[6]. Transition probabilities were limited during the later non-ambulatory HS transition; therefore, clinical expert validation through elicitation techniques were applied.
- **Patient utility values** were sourced from literautre[7] using EQ-5D-5L estimates. Utility values in the ambulatory HSs were double that in any of the non-ambulatory HSs.
  - In the absence of disutility of night-time ventilation after LOA, a 5% disutility was applied to relevant HSs based on clinical opinion.
- **Caregivers utility data** were also drawn from literature[8], with clinical validation where data were unavailable. Given the burden of DMD, 2 caregivers were considered.

The model simulated the long-term impact of givinostat over a life-time horizon, at 3.5 discount rate applied annually.

RESULTS

Based on the Markov model (Figure 1), **givinostat is estimated to extend the time spent in the ambulatory HSs**, which are associated with higher utility values, demonstrating potential benefits for both patients and caregivers.

- The model estimates **3.2 additional life years gained (LYG)**, and **7.24 quality adjusted life years (QALYs) gained** with givinostat vs. the model comparator (corticosteroids) considering patients and caregivers quality of life (QoL), driven by the extended time spent in high utility ambulatory HSs
- The model simulates that givinostat **extends the average duration that patients remained in ambulatory HSs by 4.4 years**; 2.7 years in Early ambulatory HS and 1.7 years in the Late Ambulatory HS, thereby showing the potential to delaying DMD patients' disease progression.

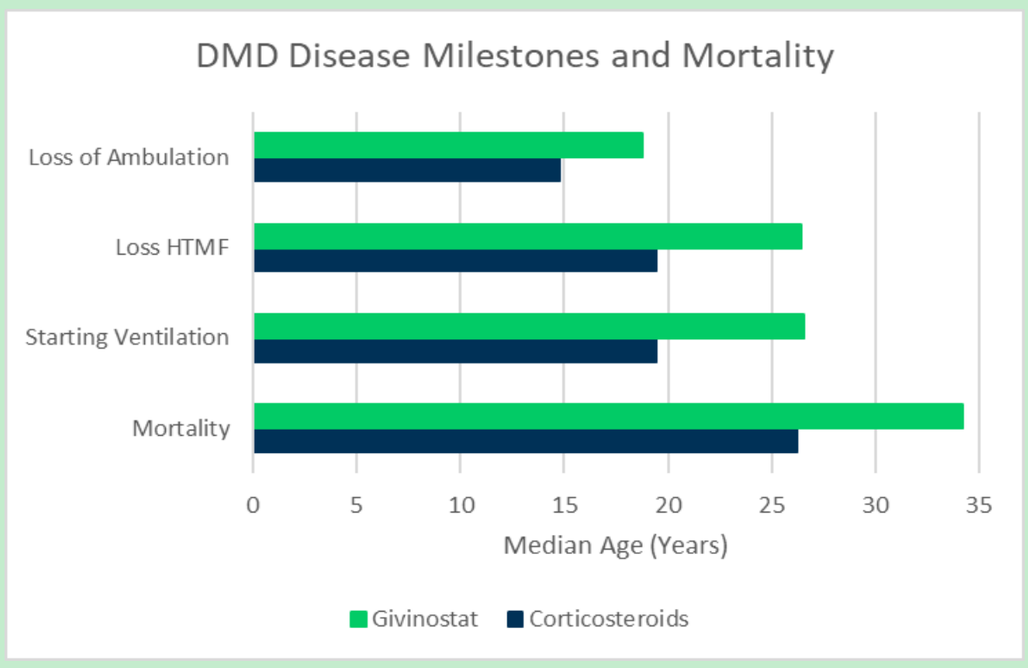


Figure 2. Model Predicted Median Age of Disease Milestone or Mortality
(adapted project Hercules)

Modelled DMD disease milestones:

The model shows an estimated **givinostat median age to LOA of 18.75** vs. 14.75 years with corticosteroids. **Loss of hand-to-mouth-function (HTMF) and starting ventilation, were also estimated to be delayed** (median age of Loss of HTMF: 26.42 vs. 19.42; median age starting ventilation: 26.58 vs. 19.42 years - Figure 2).

Modelled Survival:

The model predicts that **givinostat patients have longer survival** compared to those patients treated with corticosteroids alone (givinostat median age of death was estimated at 34.24 years vs. 26.25 years with corticosteroids). In the model, over a third of givinostat treated patients were expected to be alive at 40 years compared to just 12% of the model comparator.

Modelled Patient Quality of Life:

Model results show a substantial decline in health-related quality of life (HRQoL) as patients lose the ability to walk.

Modelled Caregivers' Quality of Life:

The model shows that as patients remained longer in ambulatory HS, caregivers benefited from higher utility values for longer.

CONCLUSIONS

Model results shows that givinostat treatment has the potential to slow disease progression, to delay relevant DMD milestones, to provide longer survival and to improve both patient and caregiver quality of life resulting in additional QALYs gained.

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This poster presents the results of the cost effectiveness model based on the Hercules model adapted to givinostat. Givinostat is not yet approved in the EU

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