Twenty Years of Clinical Trials in Duchenne Muscular Dystrophy: A Low Clinical Drug Development Success

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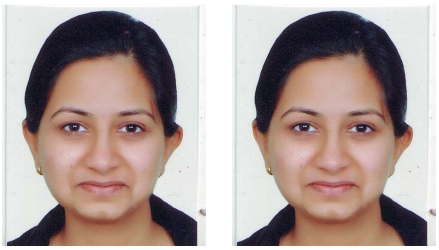


PRESENTED AT:

BACKGROUND

•Over the last decade drug development and treatment of rare diseases have considerably expanded in part due to financial support and incentives provided by governments, regulators, and nonprofit organizations

•Duchenne muscular dystrophy (DMD), a severe type of muscular dystrophy is among the most common rare diseases with no known cure[1]

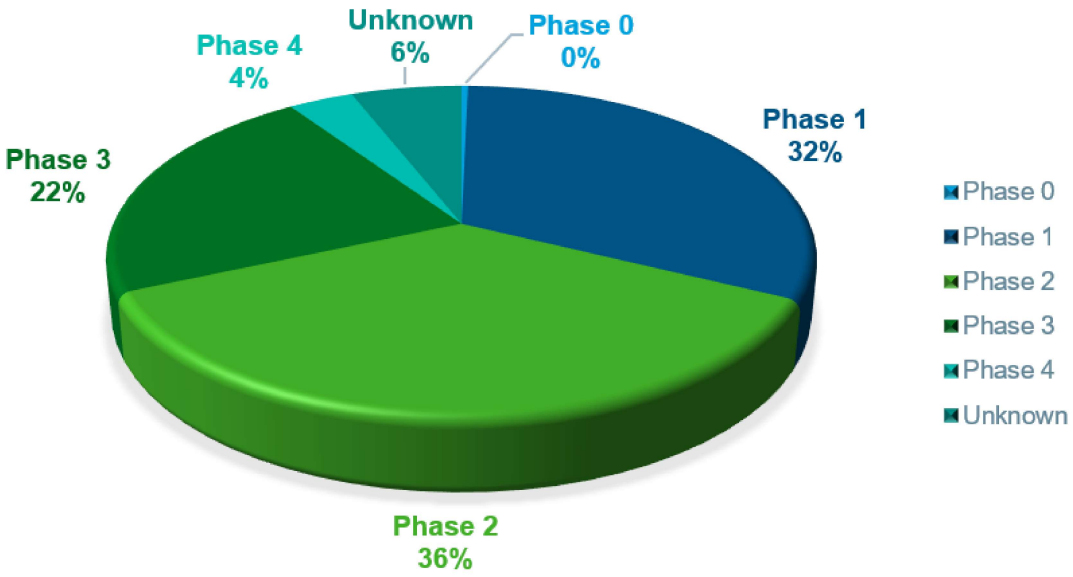
•Drug development in DMD is particularly challenging, and only four compounds are approved by the FDA[2]

DISTRIBUTION OF DMD TRIALS BY CLINICAL PHASE

- Two eighty-five trials assessing eighty-six compounds and sixty-four non-pharmacological interventions (devices and cell therapies) were identified

- One trial was identified under Phase 0

- Ninety-one (31.9%) were phase 1 trials, 103 (36.1%) phase 2, 63 (22.1%) phase 3, and 10 (3.5%) phase 4

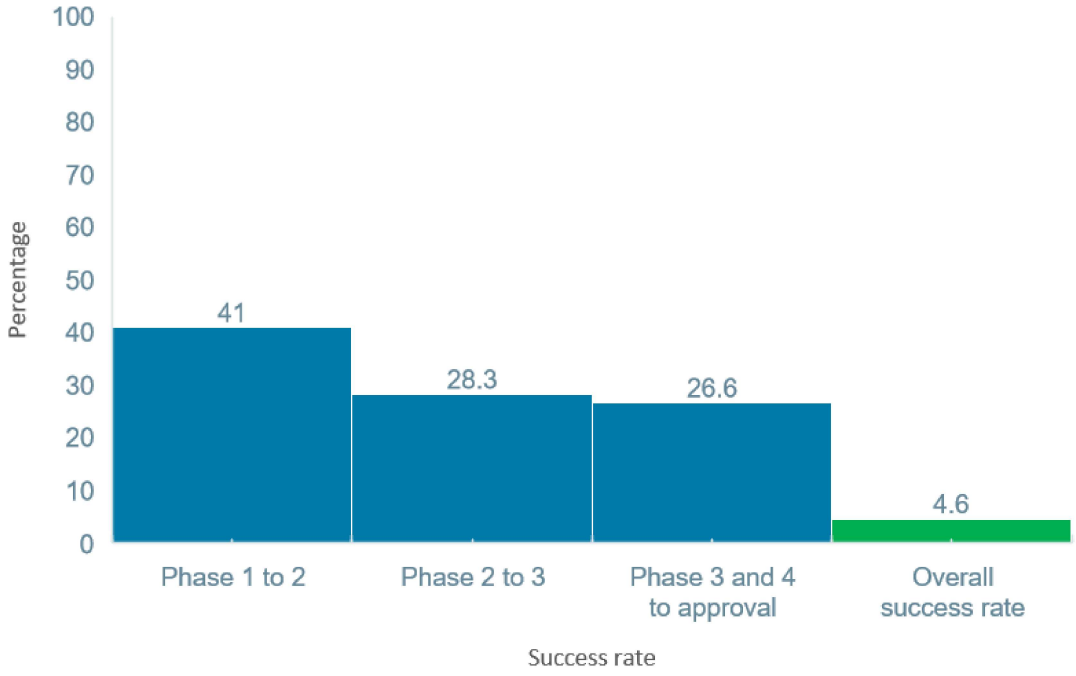


SUCCESS RATE

•The success rate was:

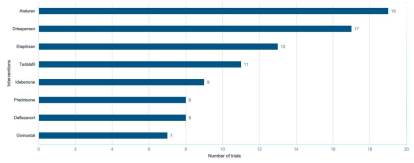
- 41 % from Phase 1 to Phase 2
- 28.3% from Phase 2 to Phase 3
- 26.6% from Phase 3 and 4 to approval

•The overall success rate was 4.6%



RANKING OF MOST FREQUENTLY EVALUATED INTERVENTIONS

•The most frequently studied compounds were Ataluren, Drisapersen, Eteplirsen and Tadalafil



OBJECTIVE AND METHODS

Objective:

To describe the landscape of DMD therapeutic development and critically explore the reasons for compound attrition in the different stages of drug development, from phase 1 to phase 4

Methods:

•All DMD clinical trials registered in the WHO International Clinical Trials Search Portal, from inception to Dec 2020 were screened and analyzed

•Two authors independently selected and extracted data

•Success rate in a trial phase was calculated as the number of compounds that progressed to the next trial phase divided by the number of compounds in that phase

•The overall success rate was calculated as the ratio between the number of compounds that receive regulatory approval and the total number of compounds

DISCUSSION

•The present study was undertaken to characterize the clinical development of therapeutic interventions in DMD and understand their evolution over time through an analysis of clinical trials registered in the ICTRP

•The number of registered trials per year increased throughout this time

•Most registered trials were Phase 2 trials

•There is a limited footprint of industry funding sources in DMD, with 53.3% being funded by the industry, exclusively or not.

•The overall success rate was only 4.6%. The reasons for lack of efficacy in well-conducted trials must be accessed to improve the success rate for drug development.

•Limitations:

- Data presented here only focus on registered trials.
- Phase 1 trials and trials evaluating complementary medicines and related therapies may be underrepresented
- There is a considerable amount of unsubmitted or missing data for certain data fields, which limits the decisiveness and interpretability of the analyses[3]

CONCLUSION

•Although DMD is a rare condition, 285 trials were identified in a comprehensive clinical trial registry

•We found a very low trial success rate

•There is a significant gap between drug discovery and development success rates that warrants improvement and careful appraisal of this life-threatening disease

DISCLOSURES

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REFERENCES

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3. Viergever RF, Ghersi D. The quality of registration of clinical trials. PLoS One. 2011;6(2):e14701. doi:org/10.1371/journal.pone.0014701