INPLASY

Antisense Oligonucleotides for Duchenne Muscular Dystrophy: Rapid Systematic Review of Phase 3 Trials

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202470031

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 09 July 2024 and was last updated on 09 July 2024.

INTRODUCTION

Review question / Objective In patients of DMD (P), do FDA approved Antisense Oligonucleotides (I) in comparison to placebo or standard care (C) improves biological or histological or clinical outcomes (O) based on data from phase 3 clinical trials (S)?

Rationale Four Antisense Oligonucleotides (AONs) with conditional FDA approval are being assessed in ongoing phase 3 trials. Preliminary phase 1/2 data of AONs is suggestive of breakthrough in treatment of DMD. The study aims to synthesize evidence emanating from phase 3 clinical trials.

Condition being studied Duchenne Muscular Dystrophy (DMD) is a fatal genetic disease affecting 1/5000 boys. Current standard of care is corticosteroid treatment which delays disease progression but causes significant adverse effects. DMD occurs mostly due to whole exon deletions or duplications in DMD gene on X-chromosome with 73% of major deletions occur in primary hot spot located between exons 43 and 55.

METHODS

Search strategy PubMed, EMBASE and Cochrane Library will be searched. Synonyms and database specific controlled vocabulary for keywords - DMD and AONs using appropriate Boolean operator. Indicative search strategy: ("Duchenne Muscular Dystrophy" OR DMD) AND (eteplirsen OR golodirsen OR viltolarsen OR casimersen OR "exon skipping" OR "antisense oligonucleotide" OR Morpholinos OR "Phosphorodiamidate Morpholino Oligomers").

Participant or population Patients with DMD.

Intervention FDA approved AONs.

Comparator Placebo or standard care.

Study designs to be included Phase 3 clinical trials.

Eligibility criteria Phase 3 clinical trials with a prospectively registered trial protocol.

Information sources PubMed, EMBASE and Cochrane Library databases.

Main outcome(s) Biological outcomes: PCR assessed exon skipping; Histological outcomes: Dystrophin level; Clinical outcomes: Distance covered in 6 Meter Walking Test, Predicted Forced Vital capacity, Ability to walk or rise from floor, age at loss of ambulation.

Data management The search results will be uploaded into RAYYAN web app for selection of eligible studies. All authors will independently collect study details and outcomes data using a predetermined form designed for this purpose. Study details will be entered into the 'Characteristics of included studies' tables.

Quality assessment / Risk of bias analysis Risk of bias will be done by Cochrane RoB tool.

Strategy of data synthesis Metanalysis, if feasible, will be conducted; failing which narrative synthesis of results will be done.

Subgroup analysis Subgroup analysis, if indicated will be done.

Sensitivity analysis Sensitivity analysis, if indicated, will be done.

Country(ies) involved India.

Keywords Duchenne Muscular Dystrophy, antisense nucleotides, morpholinos.

Dissemination plans Systematic Review will be published in a peer reviewed journal.

Contributions of each author
Author 1 - Manish Kumar.
Author 2 - Shilpa Singh.