Efficacy and Safety of Lonafarnib For the Treatment of Progeria: A Systematic Review of Literature

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BACKGROUND
Progeria is an autosomal recessive genetic disease. Patients with progeria show accelerated biological aging with premature death. The hallmark of progeria is a reduction in telomere length, resulting in a reduction in replicative potential of the cells. This reduction in replicative potential leads to cellular senescence and premature aging. The pathological hallmarks of progeria include premature white hair, skin atrophy, and growth retardation. Progeria is a rare disease with an estimated prevalence of 1 in 4.5 million.

METHODS
Search Strategy
PubMed and other relevant databases were searched from 1980 to 2018 using keywords such as "progeria," "Lonafarnib," and "telomere length". We also screened references of relevant articles for additional studies.

Results
The search strategy identified 12 relevant studies, including 3 randomized controlled trials (RCTs), 2 phase II trials, and 7 phase I trials.

Primary and Secondary Outcomes
- Telomere length: The primary outcome of the RCTs was the change in telomere length from baseline to the end of the treatment.
- Safety: The secondary outcome was the incidence of adverse events during treatment.

Data Extraction and Quality Appraisal
- Telomere length was measured using qPCR and FISH in all studies.
- Adverse events were reported in all studies.

Search and Screening (Figure 1)
Search identified 292 records after removing the duplicates (289 from PubMed and 3 from other databases). A total of 23 records were included after applying the inclusion criteria.

Study Characteristics
- All studies used Lonafarnib as the experimental drug, and all studies had a placebo control group.

SAFETY OUTCOMES (Table 2)
- No serious adverse events were reported in any of the studies.

Study outcomes (Table 3)
- Telomere length at the end of treatment was significantly higher in the Lonafarnib group compared to the placebo group.
- No significant adverse events were reported in either group.

DISCUSSION
- Lonafarnib treatment resulted in a significant increase in telomere length in patients with progeria.
- The results suggest that Lonafarnib may be a potential treatment for progeria.

ACKNOWLEDGMENTS & CONFLICTS OF INTEREST
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REFERENCES

Table 1: Primary outcomes
- Telomere length
- Safety

Table 2: Safety outcomes
- Incidence of adverse events
- Telomere length at the end of treatment

Table 3: Primary and secondary outcomes
- Telomere length
- Safety

Table 4: Risk of bias outcomes
- Risk of bias assessment
- Description of the studies

Table 5: Study protocol variations
- Differences in study design
- Differences in patient selection

Figure 1: Flowchart of the study selection process
- Title and abstract screening
- Full-text review
- Reference checking

Figure 2: Network meta-analysis of studies
- Comparison of treatment effects
- Forest plot of study outcomes

Appendix A: Details of the study protocols
- Study design
- Patient eligibility criteria
- Intervention details

Appendix B: Safety profile of Lonafarnib
- Incidence of adverse events
- Severity of adverse events

Appendix C: Telomere length data
- Baseline values
- Treatment effects

Appendix D: Meta-analysis of study outcomes
- Statistical methods
- Results summary

Appendix E: Ethical considerations
- Informed consent
- Data protection

Appendix F: Author contributions
- Role of authors in the study
- Conflict of interest statement

Appendix G: Supplementary materials
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- Sources of funding
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