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Emerging treatments for Leber Hereditary Optic Neuropathy and Retinitis Pigmentosa

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INTRODUCTION

Leber Hereditary Optic Neuropathy (LHON) and Retinitis Pigmentosa (RP) are rare-inherited diseases causing blindness with few treatments available within the European Union (EU). Raxone (idebenone) is the only approved medicinal product (MP) to treat LHON. Luxturna (voretigene neparvovec) is the only approved MP to treat RP.

AIMS

To understand emerging patterns pursued by pharmaceutical companies when developing medicinal products to treat LHON and RP.

METHOD

Phase I: MPs for LHON and RP were identified from the EU CLINICAL TRIALS REGISTER and from the US NATIONAL LIBRARY OF MEDICINE DATABASE OF CLINICAL TRIALS. Prospective treatment protocols for LHON and RP were suggested based on mutation-specific MPs and mutation non-specific MPs.

Phase II: Clinical development programs (CDPs) of MPs studied for LHON and RP were reviewed and analysed using descriptive statistics. Emerging patterns in primary endpoints studied between 2006 and 2018 were identified and compared

Phase III: A review of available regulatory pathways within the EU to obtain a license for orphan MPs was carried out.

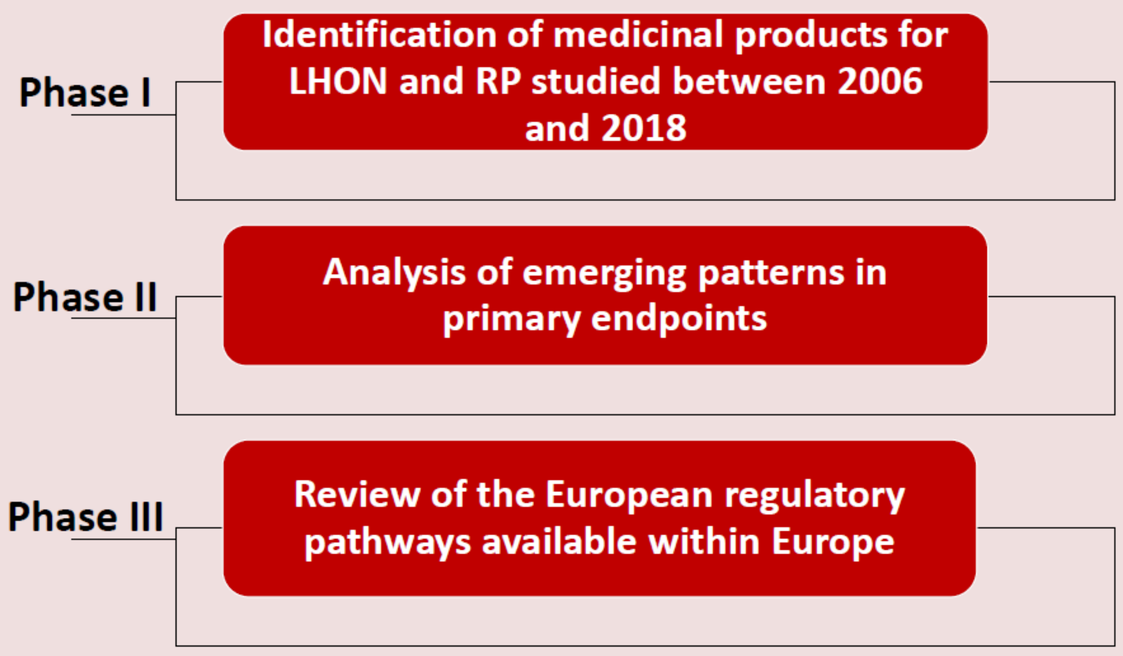

Figure 1 Overview of the methodology

RESULTS

Nine MPs studied to treat LHON and 24 MPs to treat RP were analysed. Out of 9 MPs to treat LHON, 5 were included in the prospective treatment protocol. Out of 24 MPs to treat RP, 12 were included in the prospective treatment protocol.

The included MPs for LHON and for RP are shown in Table 1.

The most common endpoints studied in CTs were change in visual acuity (n=6) for LHON and change in visual field (n=8) for RP.

Raxone was authorised under exceptional circumstances for LHON in 2015 and protocol assistance was requested during its development. Luxturna was granted a full marketing authorisation for RP in 2018 after protocol assistance was requested twice during its development.

LHON	
Non-mutation specific	**Mutation specific**
Raxone®	**GS010 (m.11778G>A)**
Cysteamine bitartrate	
EPI-743	
Autologous-bone marrow stem cells	

RP	
Non-mutation specific	**Mutation specific**
Brimonideine Tartarte	**Luxturna (RPE65)**
Levodopa-Carbidopa	**QLR091001 (RPE65)**
Fluocinolone Acetonide	
jCell	**CPK850 (RLBP1)**
Bone marrow-derived mesenchymal stem cells	**AVV-RPGR (RPGR)**
Autologous bone marrow-derived mononuclear stem cells	**Valproic Acid (autosomal dominant RP)**
NT-501	

Table 1 Medicinal products included in prospective treatment protocols for LHON (N=5) and RP (N=12)

CONCLUSION

An increased number of clinical trials associated with an increased number of drug classes explored between 2006 and 2018 have been noticed. New treatments specifically addressing mutated genes are being developed to treat LHON and RP. Only one MP for LHON and one MP for RP are currently available within the EU market and an unmet medical need is present.