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Emerging Treatments for Retinitis Pigmentosa

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INTRODUCTION

Retinitis Pigmentosa (RP) is a class of rare-inherited retinal dystrophies which can lead to blindness and is characterised by pigment deposits predominantly present in the periphery of the retina. The hereditary pattern of RP follows a Mendelian inheritance pattern. The onset of RP typically occurs during the early teenage years with difficulties in dark adaptation, concurrent nyctalopia and reduced visual field (VF) which leads to tunnel vision and gradual reduction in central vision with a risk of blindness. Currently, no standard treatment for RP is available.

One medicinal product (MP), Luxturna, which consists of voretigene neparvovec, a gene transfer vector, is authorised in the European Union (EU) and United States (US) to treat patients with inherited retinal dystrophies, caused by biallelic RPE65 mutations, and who have sufficient viable retinal cells.

AIMS

To understand emerging patterns pursued by pharmaceutical companies when developing medicinal products to treat RP and to propose prospective treatment protocols for RP.

METHOD

Figure 1 Overview of the methodology

Phase I: Investigational medicinal products (IMPs) for RP were identified using the EU CLINICAL TRIALS REGISTER and the US NATIONAL LIBRARY OF MEDICINE DATABASE OF CLINICAL TRIALS. Clinical trials (CTs) registered on CT databases between January 2006 and November 2018, evaluating a MP and studying efficacy primary endpoints were included in this study.

Prospective treatment protocols for RP were suggested according to the nature of the active substance (chemical, advanced therapy MPs and growth factors) and mutation-specific MPs and mutation non-specific MPs.

Phase II: Clinical Development Programs (CDPs) of included IMPs were analysed and compared, focusing on primary and secondary endpoints.

RESULTS

Initially, 49 CTs for 24 IMPs for RP were included. Out of 24 IMPs, 14 were Advanced Therapy IMPs (ATIMPs) (8 gene therapy and 6 somatic therapy), 8 were small molecules and 2 were growth factors. Twelve IMPs (5 small molecules, 6 ATIMPs and 1 growth factors) were included in the proposed treatment protocol for RP as in phase II and phase III of development. Only Luxturna, was authorised via a centralised procedure. The included IMPs for RP were QLT091001, valproic acid, brimonidine tartrate, levodopa-carbidopa, fluocinolone acetonide, voretigene neparvovec-rzyl (Luxturna), CPK850, AAV-RPGR, jCell, bone marrow-derived mesenchymal stem cells, autologous bone marrow-derived mononuclear stem cells and NT-501 (Table 1).

The most common safety endpoint for RP in CTs was incidence of adverse events (n=15), and the most common efficacy endpoint for RP in CTs was change in visual field (n=8), followed by best corrected visual acuity (n=6) and change in visual acuity (n=5).

Drug Category	Mutation specific	Non-mutation specific
Small Molecules	QLT091001	Brimonidine Tartrate
	Valproic Acid	Levodopa-Carbidopa
		Fluocinolone Acetonide
Advanced Therapy Medicines	Luxturna	jCell
	CPK850	Bone marrow-derived mesenchymal stem cells
	AVV-RPGR	Autologous bone marrow-derived mononuclear stem cells
Growth Factors	N/A	NT-501

Table 1 Investigational medicinal products included in prospective treatment protocols for RP (N=12)

CONCLUSION

Two main patterns have been observed: (i) the number of CTs carried out to evaluate ATIMPs is increasing from 2009, and currently 13 ATIMPs are under evaluation (ii) specific mutations are being addressed through the development of gene therapy MPs (e.g. Luxturna for RP) and small molecules (e.g. QLT091001 for RP). Important advances in research have been made, and research is moving forward in evaluating new targeted treatments which will benefit patients suffering from RP. The proposed prospective treatment protocols for RP may assist in the development of treatment for RP.