INTRODUCTION

X-linked retinitis pigmentosa (XLRP), a form of inherited retinal dystrophy, is a rare eye disease associated with the progressive loss of photoreceptors. XLRP is among the most aggressive forms of retinitis pigmentosa, affecting approximately 15% of all cases, leading to legal blindness in the third or fourth decade of life.1

• As an X-linked recessive disorder, XLRP primarily affects men. Women who are heterozygous for an XLRP mutation often experience unaffected faces, but some female carriers can experience significant visual symptoms, a phenomenon thought to be related to variable X-inactivation patterns.2

• Approximately 70-80% of XLRP cases are caused by mutations in the RPGR gene; the remaining 20-30% are caused by mutations in the RPGRIP1 gene.3

• For inherited retinal diseases such as XLRP, genetic testing is strongly recommended to provide a definitive diagnosis.4

• No treatment is currently available for XLRP. The recommended management includes use

• of low-vision aids, treatment of the complications (e.g., cataract, uveitis macular edema), and blindness rehabilitation strategies.4

• United published data are available that describe detailed aspects of the XLRP patient journey (including assessment, genetic testing, diagnosis, and management), there is a need for a more real-world understanding of the current standards of clinical practice and the potential obstacles to diagnosis and genetic testing.

• Potential barriers for XLRP emerge, early diagnosis and access to genetic testing for patients and her family members is of utmost importance, it will offer additional insights into the patient journey. The EXPLORE XLRP study interviewed retina specialists (n=20) and geneticists (n=20) in five European countries (Germany, France, Italy, Spain, and the United Kingdom) to provide insights on patients with XLRP (heterozygous), to better understand the pathways by which patients in Europe with XLRP are referred to these specialists for diagnosis, and to examine the impact of COVID-19 on patient management.

METHODS

• EXPLORE XLRP was an exploratory, cross-sectional, physician conducted in Germany, France, Italy, Spain, and the UK.

• Retina specialists and geneticists in these countries were identified who had at least 5 years’ experience managing or seeing patients with XLRP, and who were responsible for the recent management of patients with XLRP (heterozygous) or who were responsible for the genetic testing of patients with XLRP in their respective countries.

• Retina specialists provided anonymised information for four recent patients diagnosed with XLRP who had a direct relation to their management, including details of the diagnostic and referral process and decisions to pursue genetic testing.

• The anonymised patient information was collected through an online survey completed by the retina specialists and geneticists in their respective countries.

• Individual face-to-face interview telephone interviews were then conducted with the retina specialists and geneticists to capture their perspective on on-management approaches for patients with XLRP.

RESULTS

• A total of 20 retina specialists and five geneticists from Germany, France, Italy, Spain, and the UK participated in the study (four retina specialists and one geneticist from each country).

• Patient information was collected for 80 patients (16 from each country).

• The retina specialists and geneticists interviewed reported that their patients with XLRP were mostly male (91%) and that 57% were aged 18-40 years.

• The retina specialists estimated that it usually took longer than 6 weeks to receive the results of genetic testing, and some patients waited up to 6 months to receive test results (Figure 4).

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• Once diagnosed, patients are provided with information about the disease, how it progresses, and their prognosis.

• Patients are encouraged to speak to a genetic counsellor to understand the hereditary nature of the disease.

• The range of monitoring is highlighted, especially given the complications that can arise.

• Retina specialists reported seeing patients with XLRP typically once or twice a year for consultations.

Diagnosis and genetic testing

• The retina specialists interviewed indicated that more than half (58%) of their patients with XLRP were initially referred to the retina specialist without a specific suspicion of XLRP.

• Genetic testing was used as part of XLRP diagnosis in 78% of patients; among the five countries, the lowest rate of genetic testing (50%) was reported in France.

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• Prior to genetic testing, was undertaken, key tools used to support XLRP diagnosis included optical coherence tomography, electrophysiology, fundus autofluorescence, visual acuity testing, and static perimetry.

• Despite barriers to genetic testing (e.g., costs, long waiting times for results), physicians agreed that genetic testing is helpful in predicting disease progression and to allow patients the option of participating in clinical trials.

• Additional barriers to reliable genetic testing included the distances some patients needed to travel, the fact that no treatment is available for the disease, and the concerns of some patients regarding identification of mutations in the family.

• The clinical experts generally recommend that the family members of patients with suspected or confirmed XLRP should also be genetically tested.

CONCLUSIONS

• Early diagnosis is important for patients to be able to better understand the impact of their diagnosis on their life and family, and also to allow them the option of participating in clinical trials.

• The pathways by which patients with XLRP in these five European countries agreed on retinal specialists and geneticists are complex, length, and vary considerably by country.

• XLRP diagnosis was confirmed by genetic testing for the majority of patients treated by retina specialists; however, long waiting times for test results accounted for incomplete uptake, especially among older patients.

• Tele-consultations and remote management have emerged as potential solutions for the management of people with XLRP (potentially beyond) and can reduce the travel burden for patients and their caregivers/supporters.

• Although this cross-sectional survey was exploratory in nature, it provides valuable real-world insights from retina specialists and geneticists that may not otherwise be available through clinical studies or health economic research and demonstrates that diagnosis, genetic testing, and management pathways can vary considerably among patients with XLRP.

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Conflicts of interest

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Impact of the COVID-19 pandemic

• The COVID-19 pandemic led to a reduction in in-person clinic visits, which was thought to be a consequence of the fear of infection, as well as travel restrictions being imposed.

• HCPs are interested in solutions for remote management of patients, with some physicians having seen patients via video consultations.

• Ongoing barriers to successful genetic testing include the delays in obtaining test results, the costs of testing, and the potential obstacles to diagnosis and genetic testing.

• Although this cross-sectional survey was exploratory in nature, it provides valuable real-world insights from retina specialists and geneticists that may not otherwise be available through clinical studies or health economic research and demonstrates that diagnosis, genetic testing, and management pathways can vary considerably among patients with XLRP.