The Humanistic Impact of X-Linked Retinitis Pigmentosa: Results from the EXPLORE XLRP-2 Retrospective Chart Review and Cross-Sectional Survey of Patients and Caregivers in 10 Countries

HSD42

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INTRODUCTION

X-linked retinitis pigmentosa (XLRP) is among the most severe forms of retinitis pigmentosa, an inherited retinal disease.[1,2] Symptoms caused by progressive degeneration of the retina usually start in childhood, leading to legal blindness at a median age of 45 years.[2,3] In over 70% of patients, the disease is caused by variants in the RP GTPase regulator (RPGR) gene.[4] Although patients and caregivers may experience significant physical, emotional, and financial burdens, there is limited evidence on the humanistic and economic impacts of this orphan disease.[2]

OBJECTIVES

The primary objective of this study was to explore the relationship between the clinical stages of XLRP and the associated clinical, individual, and societal burdens in a real-world setting.

The secondary objectives were to describe:

- Disease pathways, including diagnosis and management sequences in XLRP within routine clinical practice
- Individual, social, and economic burdens (e.g. productivity issues, difficulties with daily functioning) associated with XLRP
- Impact of the disease on caregivers (e.g. well-being, financial impact)

METHODS

EXPLORE XLRP-2 is a non-interventional study conducted in 23 centres in 10 countries (Austria, Belgium, Finland, France, Germany, Israel, Italy, the Netherlands, Spain, and England). Participants could not enrol as both a patient and caregiver in the study.

Patient

- Male or female aged ≥12 years at screening
- Has XLRP confirmed by a retina specialist and has a predicted disease-causing sequence variant in RPGR confirmed by genetic testing
- Able and willing to give informed consent or assent, with the guidance of a legally acceptable representative (as applicable)
- No participation (current or former) in a gene therapy trial

Caregiver

- Identified by the participating patient who consented for their caregiver to be approached
- Male or female aged ≥18 years who has a personal relationship with and/or provides unpaid support or care to someone diagnosed with XLRP, e.g. spouse, partner, other relative, neighbour, friend
- Provides support or care for ≥1 hour/week
- For patients with more than one caregiver, the most impacted/involved caregiver (the main support person) was selected
- Able and willing to give informed consent

Data were collected from two sources:

1. Retrospective data (up to 5 years prior to enrolment; additionally, data from the first visit if this was earlier than 5 years before enrolment) from patients' medical records available at the sites (ophthalmology centres managing inherited retinal diseases)
2. Cross-sectional patient and caregiver surveys managed through interviews by qualified personnel at a call centre or the participating site, depending on local regulations. Surveys included both patient-reported outcomes (PRO) surveys and a questionnaire developed by the sponsor to collect data on longer-term impacts of the disease

Data were summarised using descriptive statistics:

- Continuous variables were summarised using number of patients (n), mean, standard deviation (SD), median, minimum, maximum, and 95% confidence interval (CI)
- Categorical variables were summarised using n, percent, and 95% CI
- Correlations between disease stage (Table 1) and level of burden were analysed exploratively using appropriate correlation methods. All reported p-values were non-adjusted, nominal, and exploratory

Table 1. Classification of disease stages

Disease stages*	Visual acuity		Visual field
	Decimal notation	Snellen	Diameter
Mild	≥0.32	≥20/63	≥80°
Moderate	<0.32, ≥0.125	<20/63, ≥20/160	<80°, ≥40°
Severe	<0.125	<20/160	<40°

*Based on vision status of the better eye using information from the last visit

RESULTS AND DISCUSSION

Key Demographics and Baseline Characteristics

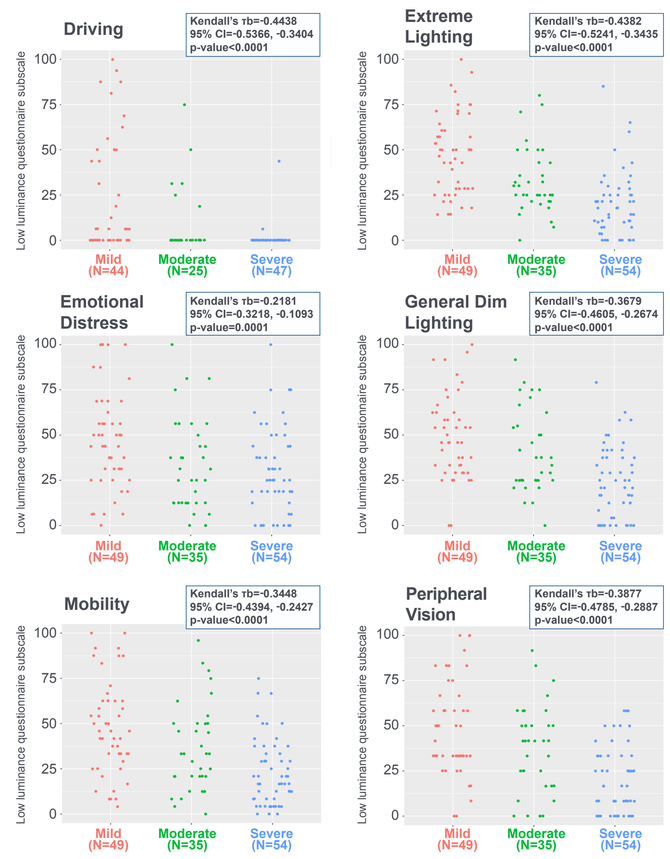
- **169** patients were included in the analyses
- **81%** male
- Mean age: **39.3 years** (SD: 17.6 years)
- **20** adolescents aged 12–17 years
- **Nyctalopia/night blindness (56%)** was the most commonly reported initial XLRP symptom
- **69** caregivers were included in the analyses
- **88%** female
- Mean age: **49.4 years** (SD: 11.7 years)
- **Caregivers** were most commonly either spouses (50.8%) or parents (41.5%) of the patients

Outcomes from Self-Reported Surveys: Patients

Modified Low Luminance Questionnaire (mLLQ)

- 138 adults (≥18 years old) responded to each domain of the mLLQ except Driving, which only had 116 respondents
- All six domains were significantly negatively correlated with the level of disease severity (Figure 1)
  - Patients with more severe disease struggle more with activities, particularly in low lighting or at night

Figure 1. mLLQ outcomes in adults

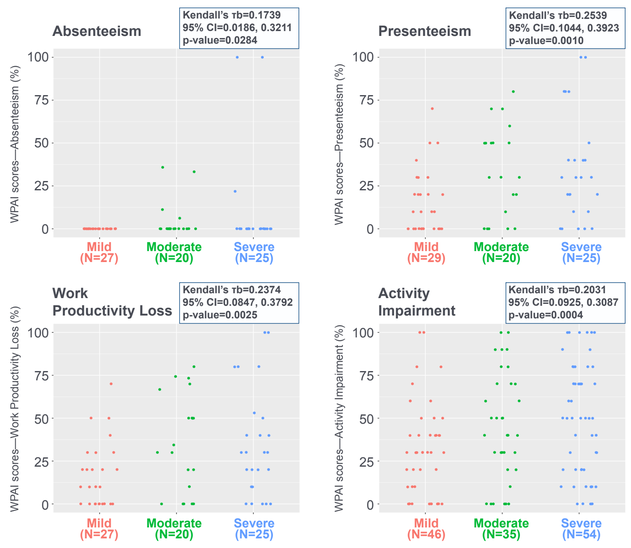


Note: mLLQ subscale scores range from 0 (maximal difficulty) to 100 (no difficulty).

Work Productivity and Activity Impairment General Health v2.0 (WPAI GH2)

- 138 patients completed the questionnaire; 76 (55.1%) were employed
  - Patients with more severe disease were less likely to be employed, but the correlation was not significant
- Employed patients with more severe disease were significantly more likely to:
  - miss time at work (absenteeism; Figure 2) (although overall absenteeism was low, and patients with mild XLRP reported no absences at all)
  - experience impairment while working (presenteeism; Figure 2)
  - have higher degrees of work productivity loss (Figure 2)
- Activity impairment scores also correlated significantly with level of disease severity (Figure 2)

Figure 2. WPAI GH2 outcomes



Note: Higher numbers indicate greater impairment and less productivity.

Hospital Anxiety and Depression Scale (HADS)

- HADS depression measures correlated significantly but weakly with XLRP stage (Table 2)
- HADS anxiety measures did not correlate significantly with disease stage (Table 3)
- 72% of patients reported no depression, and 55% of patients reported no anxiety
- Patients with moderate and severe disease reported any level of depression or anxiety more frequently than those with mild disease

Table 2. HADS depression outcomes

HADS depression score	XLRP disease stage			
	Mild (N=58)	Moderate (N=40)	Severe (N=59)	Total (N=157)
Normal (%)	46 (79.3%)	26 (65.0%)	41 (69.5%)	113 (72.0%)
Mild (%)	10 (17.2%)	5 (12.5%)	9 (15.3%)	24 (15.3%)
Moderate (%)	2 (3.4%)	7 (17.5%)	7 (11.9%)	16 (10.2%)
Severe (%)	0	2 (5.0%)	2 (3.4%)	4 (2.5%)
Significant correlation between disease stage and depression: Kendall's τb=0.1551; p=0.0034				

Table 3. HADS anxiety outcomes

HADS anxiety score	XLRP disease stage			
	Mild (N=58)	Moderate (N=40)	Severe (N=59)	Total (N=157)
Normal (%)	36 (62.1%)	23 (57.5%)	28 (47.5%)	87 (55.4%)
Mild (%)	11 (19.0%)	8 (20.0%)	17 (28.8%)	36 (22.9%)
Moderate (%)	8 (13.8%)	6 (15.0%)	12 (20.3%)	26 (16.6%)
Severe (%)	3 (5.2%)	3 (7.5%)	2 (3.4%)	8 (5.1%)
No significant correlation between disease stage and anxiety: Kendall's τb=0.0837; p=0.1166				

Patient Global Impression of Mobility and Daily Activity

- Mobility and daily activity scores significantly correlated with disease stage severity
  - Notably, almost two-thirds of patients with mild XLRP reported impact on mobility and daily activities
    - Over 90% of patients with severe disease reported an impact on both these aspects

Sponsor-Developed Questionnaire

- Clinical stage was significantly correlated with:

- 46.2% of patients reported reliance on caregiver support (stage: mild, 33.3%; moderate, 32.5%; severe, 67.8%)
- 63% reported that XLRP had an impact on career development (stage: mild, 40.8%; moderate, 77.1%; severe, 74.1%), with most reported impacts being negative
- 80.8% reported that XLRP had an impact on participation in group activities (stage: mild, 63.8%; moderate, 79.5%; severe, 98.3%), with most reported impacts being negative
- 39.4% of adult patients reported that the disease affected their financial situation (stage: mild, 26.5%; moderate, 44.1%; severe, 48.1%), with most reported impacts being negative
- 42.3% received support from social services or other compensation (stage: mild, 18.4%; moderate, 32.4%; severe, 70.4%)
- The mean number (SD) of visits to HCPs (other than a retina specialist) to discuss management of XLRP in the past year was:
  - 4.1 (8.7) to GPs
  - 7.4 (12.2) to other HCPs

GP, general practitioner; HCP, healthcare professional.

Outcomes from Self-Reported Surveys: Caregivers

Of the 65 caregivers who answered the question on employment, 72% reported being employed

- There was no significant correlation between caregiver employment and the clinical stage of XLRP in the patient they cared for

Caregivers reported a mean (SD) of 28.7 (34.5) hours spent per week caring for the patient in the past year

Survey outcomes reflected an overall high level of well-being among caregivers:

EQ-5D-5L (N=64)

- Index and VAS scores did not correlate significantly with the clinical stage of XLRP in the patient
- Only caregivers of patients with moderate or severe XLRP reported severe or extreme problems with usual activities, pain or discomfort, and anxiety or depression; yet, the numbers were very low

HADS (N=65)

- Most caregivers scored within normal and mild ranges for both depression and anxiety
- Depression and anxiety scores were numerically the highest for caregivers of patients with moderate disease

CWBS-SF (N=64)

- Neither the basic human needs nor activities of daily living in caregivers correlated significantly with the clinical stage of XLRP in the patient they cared for

CWBS-SF: Modified Caregiver Well-being Scale – Short Form; EQ-5D-5L: 5-level EuroQol 5-dimension scale; VAS: visual analogue scale.

CONCLUSION

This is the first real-world study to collect data directly from patients and their caregivers on the burden of XLRP and to associate this burden with disease stage. The findings demonstrated that XLRP has a considerable impact on patients' lives, and many of these impacts correlated with disease severity.

Caregivers were mainly female (parents or spouses) and spent many hours per week supporting patients. Caregivers reported limited impact on their quality of life, with the tendency of highest distress and impact reported when caring for patients in moderate disease stage.

Our findings highlight the unmet needs of patients with XLRP and their caregivers, who are faced with significant emotional and societal burdens that increase as the disease progresses.

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DISCLOSURES

TD, ML, JV, and KP are employees of Janssen Pharmaceutica N.V., a pharmaceutical company of Johnson & Johnson.

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