# Protocol for the first global study capturing the patient-reported impact of adult-onset leukoencephalopathy with axonal spheroids and pigmented glia (ALSP) in the real-world setting using a smartphone application

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## INTRODUCTION

ALSP is a neurodegenerative disease characterized by accelerated development of neurological symptoms such as cognitive impairment, moderate to severe motor dysfunction and neuropsychiatric complications[1,2]. ALSP is a rapidly progressive, debilitating, autosomal dominant inherited disorder that results in diminishing quality of life and shortened life span.

ALSP is an underdiagnosed disorder and often misdiagnosed in the early stages as Alzheimer's disease, frontotemporal dementia, multiple sclerosis, adult-onset leukodystrophy or familial leukoencephalopathy.

At present, there are no FDA-approved therapies for ALSP; available treatments are symptom targeted and offer limited, short-term efficacy. Moreover, they do not target the most impairing symptoms, nor do they decelerate the progression of the disorder.

ALSP is a rare, global disease with a NORD 2021 estimated prevalence of 10,000 in the United States and a similar point prevalence and incidence in Europe and Japan.

ALSP is caused by loss of function mutations in the *CSF1R* gene that elicit structural abnormalities and pathophysiology of axons and microglia and demyelination of white matter of the brain.

Since there are no published prospective studies on the natural history of ALSP, descriptions of phenotypic features are limited and derived primarily from small case series and single case reports.

## OBJECTIVES

As with many rare diseases, there is little patient-reported data to understand and address patient needs. This study explores the impact of ALSP in the real world, from the patient and caregiver perspectives including:

(1) Demographic and clinical characteristics of the ALSP population

(2) Treatment and medical care characteristics and associated costs as well as quality of life impact

## METHODS

The ALSP Registry launched January 31, 2022. This is, to our knowledge, the first global study capturing the patient-reported impact of ALSP.

This is an international two-year prospective, observational digital study with confirmed diagnosis of ALSP or colony- stimulating factor 1 receptor (*CSF1R*) gene mutation.

The study is administered via mobile app and caregivers can participate on behalf of a patient when necessary.

Registry is active in the following countries: Germany, the Netherlands, the UK, and the USA, with the USA and the UK currently the most active countries.

Recruitment is via patient associations, word of mouth, and referral from physicians.

Participants use a bespoke smartphone application (ALSP Registry) to check eligibility, provide informed consent, and contribute data.

Data entry is as follows:

(1) Screening questionnaire;

(2) Background surveys upon enrollment covering demographics, diagnosis, and family history;

(3) Regular (quarterly, biannual, or annual) completion of surveys covering current symptoms and treatments, medical care including associated costs, and work/study impacts;

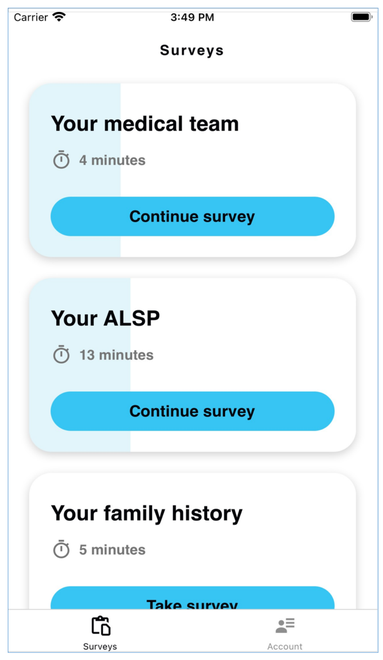
(4) Quarterly completion of the EQ-5D-5L, a generic patient-reported outcomes instrument.

Analyses are planned for when the study has been running in a majority of the countries for 12 and 24 months.

Ethical approval of the study was obtained from a central institutional review board.

## RESULTS

Participant recruitment started in January 2022.

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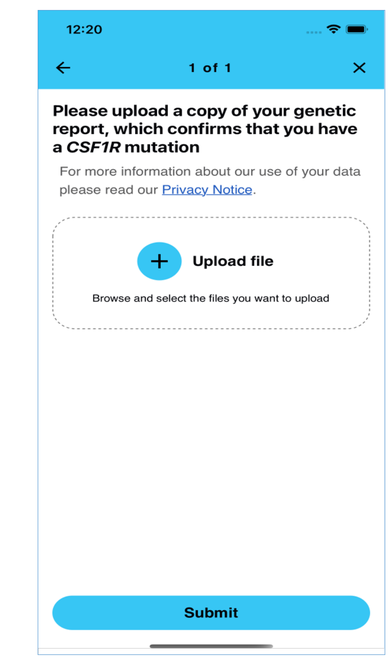
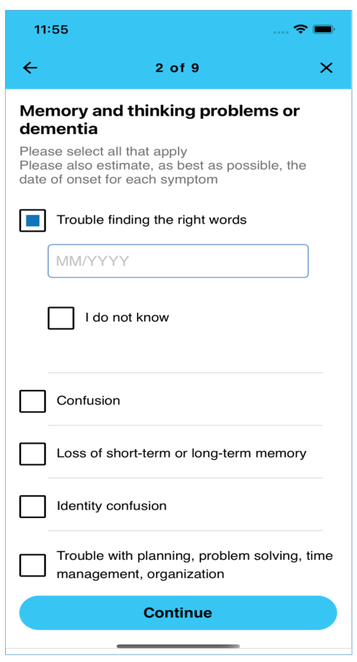
## CONCLUSIONS

To our knowledge, this is the first global study capturing the patient-reported impact of ALSP. Collecting data directly from participants enables those with ALSP to share their own experiences of living with the condition. It will be the basis for scientific collaboration and will foster multidisciplinary knowledge on ALSP to improve patients' health outcomes.

The ALSP Registry will also support enrollment for the ongoing observational natural history study and the planned VGL 101 Phase 2 clinical trial in ALSP.

**ALSP Registry**




## REFERENCES

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[2]Papapetropoulos S et al. Adult-onset Leukoencephalopathy with axonal spheroids and pigmented glia: review of clinical manifestations as foundations for therapeutic development. Front Neurol 2022;12:788168.

## DISCLOSURES

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## ACKNOWLEDGEMENTS

The study team wishes to thank the patients and families who are contributing data to the registry.