PATIENT INFORMATION SHEET

TÍTULO DEL ESTUDIO: La encefalitis mediada por anticuerpos LGI1: síntomas, biomarcadores y mecanismos de la fase crónica de la enfermedad

Title: Antibody-mediated LGI1 encephalitis: symptoms, biomarkers, and mechanisms of the chronic phase of the disease

PRINCIPAL INVESTIGATOR COORDINATING CENTER:

Dr. Josep Dalmau
Neuroimmunology Unit, Neurology Department
CENTER: Hospital Clínic de Barcelona (Barcelona, Catalonia)
Neuroimmunological Diseases Research Group
CENTER: IDIBAPS-Hospital Clínic, Barcelona

CO-PRINCIPAL INVESTIGATOR
Dr. Lorena Rami
Alzheimer's and Other Cognitive Disorders Unit
CENTER: IDIBAPS-Hospital Clínic, Barcelona

INTRODUCTION

We are reaching out to inform you about a research study in which you are invited to participate. The study has been approved by a Research Ethics Committee in accordance with current laws. If you need any clarification regarding any questions that may arise after the explanation, you can speak with any member of the team or with Dr. Josep Dalmau (contact phone number 93 227 1738), who is responsible for coordinating the project. Additionally, you may consult with anyone you deem appropriate.

VOLUNTARY PARTICIPATION

Participation in this study is voluntary, and you may choose not to participate or change your decision and withdraw your consent at any time without affecting your relationship with your doctor or the treatment you receive.

OVERVIEW OF THE STUDY:

You are invited to participate in a research study led by Dr. Josep Dalmau and Dr. Lorena Rami from the Neurology Department at Hospital Clínic Barcelona.

The disease you have is called antibody-mediated LGI1 encephalitis. Autoimmune encephalitis comprises a group of neurological diseases in which one of the body's defense systems (antibodies) attacks the brain cells (neurons), primarily in the communication area between neurons (synapses and neuronal receptors). These alterations cause neurological problems that may include memory loss, behavioral changes, or epileptic seizures. One of the most common autoimmune encephalitis types, called anti-LGI1 encephalitis, was discovered by the principal investigator, Dr. Dalmau, in 2010. Since then, a total of 16 autoimmune encephalitis types have been discovered, most by Dr. Dalmau. All these diseases are potentially lethal but can be cured if diagnosed and treated early. Although the initial, more evident symptoms can quickly improve with the treatments used, a

common problem is that many patients are left with residual symptoms that improve slowly or persist permanently. This phase is often referred to as the chronic phase of the disease. One of the encephalitis types with the most problems in the chronic phase is precisely anti-LGI1 encephalitis.

It is known that people with this type of autoimmune brain disease have cognitive, behavioral, and sleep habit alterations that persist for months after the acute phase of the disease. However, we do not exactly know the cause of these alterations, the most appropriate treatment, the need to prolong immunotherapy, or the factors that help predict the patients' recovery prognosis.

The general purpose of this research is to improve our understanding of the symptoms throughout the disease. This evaluation will be conducted during hospital visits. During the visits, several specialists (neurologist, psychiatrist, neuropsychologist, sleep specialist) will talk with you and your family member and perform medical tests to assess the presence of cognitive (memory, attention, perception, and language), psychiatric (mood and behavior variations), and sleep problems. An electroencephalogram, an electromyogram, and a sleep test will be performed at each visit, and a brain MRI will be conducted at the second visit. Additionally, a lumbar puncture (LP) will be performed at the initial visit and the third visit. All these tests will be conducted in the hospital and are part of the usual practice for monitoring encephalitis recovery, but in this study, they will be done in a more planned manner and will include the analysis of a larger number of biological variables.

Moreover, this study includes a cognitive rehabilitation program in collaboration with the Institut Guttmann (with whom we already have experience in their cognitive stimulation program in patients with the type of encephalitis you have but not in a systematic way, as we will now develop). This rehabilitation program will be carried out during the first 6 months of the study.

In total, participation in the study includes: 3 visits over 12 months.

- For the 3 in-person visits, you will be asked to travel to Hospital Clínic de Barcelona (first visit, second visit at 6 months, and third visit at 12 months; this will not incur any cost to you). Each of these visits will be completed over 2 days and includes the tests indicated in the diagram below:

- The MRI will only be conducted once, during the second visit (V2). The lumbar puncture (LP) will be performed whenever possible during both the first visit (V1) and the third visit (V3).
- The cognitive rehabilitation program (conducted online from home) aims to enhance the recovery of cognitive functions (attention, memory, mental processing speed) and help you return to your usual life sooner. You will perform exercises tailored to your needs by a cognition

specialist using your computer or an iPad tablet that we will provide, according to your preference. Sessions will last 45 minutes, twice a week during the first 3 months of the study, and once a week during the following 3 months.

Throughout the study, you will have telephonic or video-conference support from a neuropsychologist on the research team who will address any questions or issues regarding both cognitive evaluation exercises and tasks with the portable device.

Data collection will occur at all follow-up visits by your doctor. Additionally, clinical data on the progression of your disease will be collected to correlate with study outcomes.

A total of 20 individuals from across Spain are expected to participate in this study. You will be asked to promptly report any neurological symptoms that occur during the study and may be significant.

The data obtained in this study will be compared with data from patients with the same disease, antibody-mediated LGI1 encephalitis, who did not receive cognitive rehabilitation, to investigate the efficacy of this treatment. We will also explore whether the detected alterations in these patients are related to abnormalities in synapses or connections between neurons.

BENEFITS AND RISKS ASSOCIATED WITH YOUR PARTICIPATION IN THE STUDY

It is possible that you may not derive specific benefits from participating in the study. However, the study has been designed considering the potential benefits of an intensive cognitive rehabilitation program specifically tailored to your needs, as well as close clinical monitoring by a highly specialized team in your disease. The validation of the effectiveness of this treatment will only be possible at the end of the project and is currently speculative. On the other hand, identifying exact parameters of cognitive deficits and behavioral alterations could benefit future patients and contribute to a better understanding and treatment of this encephalitis. Additionally, you will have access to the results obtained from cognitive performance tests, clinical evaluations, neuroimaging, and neurophysiological assessments, with a detailed report of these findings.

Some tests involve possible risks, although very low in probability and also very mild:

1) Brain MRI: Some participants may experience claustrophobia or discomfort from the machine's noise, but the test can be stopped at any time.

2) Blood analysis: There is a very low risk of infection, dizziness, or bleeding, which is similar to routine blood tests.

3) EEG: Very sporadically, some participants report mild irritation on the scalp where electrodes were placed, which typically resolves within a few hours without needing intervention.

4) Lumbar puncture (LP): This common neurology procedure involves obtaining a small sample of cerebrospinal fluid from the lower back. It may cause temporary discomfort and pain in the back. Headaches occur in less than 10% of cases and typically resolve within a few days at most. Rare but possible side effects include infection, nerve root injury, and bleeding. To minimize these risks, an experienced physician will perform the lumbar puncture using conventional measures to prevent

infection or bleeding. Samples will be destroyed unless the patient signs a separate specific consent to store them.

The rest of the tests conducted in this study do not pose any health risks to the participant nor do they have any adverse effects.

ALTERNATIVE TREATMENTS

Currently, the medium to long-term treatment of autoimmune encephalitis is not clearly established. If you choose not to participate in the study, you will receive treatment according to your doctor's decision and standard practice.

CONFIDENTIALITY

Hospital Clínic de Barcelona, with VAT number 0802070C, as the data controller, informs you that the processing, communication, and transfer of personal data of all participants will comply with Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of individuals concerning the processing of personal data and on the free movement of such data, and Organic Law 3/2018, of 5 December, on the Protection of Personal Data and guarantee of digital rights. The legal basis justifying the processing of your data is the consent you give at this moment, in accordance with Article 9 of Regulation (EU) 2016/679.

Data collected for these studies will be identified only by a code, therefore no information that could identify participants will be included. Only the study doctor and authorized collaborators will be able to link your study data with your medical history.

Your identity will not be accessible to anyone else except in case of a medical emergency or legal requirement. Health authorities, the Research Ethics Committee, and personnel authorized by the study sponsor may have access to your personally identifiable information when necessary to verify study data and procedures, always maintaining confidentiality as required by current legislation.

Only encoded data will be transferred to third parties or other countries, which will never contain information that can directly identify the participant (such as name, initials, address, social security number, etc.). If such transfer occurs, it will be for the same purpose as described in the study and ensuring confidentiality.

If encoded data are transferred outside the EU to entities related to the hospital where you participate, service providers, or collaborating researchers, your data will be protected by safeguards such as contracts or other mechanisms established by data protection authorities.

In addition to the rights already provided by previous legislation (access, modification, opposition, and cancellation of data, deletion in the new Regulation), you now have the right to limit the processing of incorrect data, request a copy, or request the transfer to a third party (portability) of the data you have provided for the study. To exercise these rights or if you wish to learn more about confidentiality, you should contact the principal investigator of the study or the Data Protection Officer of Hospital Clínic de Barcelona at protecciodades@clinic.cat. You also have the right to address the Data Protection Agency if you are not satisfied.

Data already collected cannot be deleted even if you withdraw from the study, to ensure the validity of the research and comply with legal obligations and medication authorization requirements. However, no new data will be collected if you decide to stop participating.

The Investigator and the Sponsor are required to retain the data collected for the study for at least 10 years after its completion. Subsequently, personal information will only be retained by the center for health care purposes and by the sponsor for other scientific research purposes if the patient has consented to this, and if permitted by applicable law and ethical requirements.

COLLECTION AND USE OF BIOLOGICAL SAMPLES

Participation in this study involves the analysis of biological samples. If there are residual clinical samples of serum and cerebrospinal fluid (obtained during your hospitalization in the acute phase of the disease), they may be used to expand the analyses within the context of the current study. These samples will be stored identified only by a code in the Laboratory of Neuroimmunology at IDIBAPS-Hospital Clínic until their use for the objectives of this study. Once completed, any remaining samples will be destroyed unless you sign a separate consent for them to be stored and used in future research. If relevant information that could affect your health or that of your family is obtained, you will be notified if you wish.

ECONOMIC COMPENSATION

For the 3 in-person visits, you will be asked to travel to Hospital Clínic de Barcelona (first visit, second visit at 6 months, and third visit at 12 months). These or any other additional visits related to this research project will not incur any financial costs for you.

CONSENT FORM FOR ADULT PARTICIPANTS

Study Title: "Antibody-mediated LGI1 Encephalitis: Symptoms, Biomarkers, and Mechanisms of the Chronic Phase of the Disease". Version 4, February 2, 2024

I, (*participant's full name*) .....

I have read the information sheet provided to me about the study.

I have been able to ask questions about the study.

I have received sufficient information about the study.

I have spoken with: (researcher's name) .....

I understand that my participation is voluntary.

I understand that I can withdraw from the study:

- At any time.

- Without having to provide explanations.

- Without this affecting my medical care.

In accordance with the provisions of the law, I declare that I have been informed of the existence of a file or processing of personal data, the purpose of collecting such data, and the recipients of the information.

I consent to the processing of:

- ✓ My personal data for the purpose of conducting the research project..
- ✓ My personal data for the purpose of conducting similar research projects to the present one or within the same research area.

1. I freely give my consent to participate in the study:

□ YES □ NO

2. I agree to the use of the remaining clinical samples of my serum and cerebrospinal fluid from the disease diagnosis for further analysis:

□ YES □ NO

3. I wish to be informed of any research findings that may be relevant to my health:

□ YES □ NO

Participant's signature

Date: ____/____/____

Researcher's signature

Date: ____/____/____