# Characterizing Biomarkers and Associations of Clinical Outcomes in Anti-LGI1 Autoimmune Encephalitis

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## Background

- Anti-Leucine-Rich Glioma Inactivated-1 (LGI1) Autoimmune Encephalitis (AE) is a type of AE characterized by seizure activity and cognitive, behavioral, and memory disturbances[1]
- Cerebrospinal fluid (CSF) and plasma biomarkers have been adapted for monitoring disease activity and severity in individuals with neurodegenerative disease and neuroinflammatory diseases[2,3]
- There are limited studies of central nervous system (CNS) injury biomarkers and chemokines in AEs
- Cytokines play a key role in the immune regulation and inflammation seen with various autoimmune disorders
- Several studies have explored the cytokine profile of autoimmune encephalitis in the CSF, but their interpretation and comparison is challenging due to their small sample sizes and high heterogeneity[4]

## Objective

- To examine the correlation between clinical outcomes, using modified Rankin Score (mRS), Montreal Cognitive Assessment (MoCA), lab values, and clinical presentation, with blood-based biomarkers including neurofilament light chain (NfL), glial fibrillary acidic protein (GFAP), and ubiquitin c-terminal hydrolase 1 (UCH-L1) to explore their relationship to disease severity, disease progression, and as a potential prognostic makers of long-term disability or cognitive outcomes
- To address how blood-based inflammatory cytokines, such as IL-6, are related to disease activity

## Methods

- Chart review of 21 participants from the University of Colorado Hospital (UCHealth) on the inpatient neurology service and through the Autoimmune Neurology and Neuroimmunology clinics at the Rocky Mountain Multiple Sclerosis (MS) Center (RMMSC) from October 2018 to April 2024
- We utilized 16 headache controls from the RMMSC Biorepository for the Study of Neuroimmunological Disorders.
- Measurements of biomarkers were performed in duplicate using the SIMOA 4-Plex kit (Quanterix SR-X by SIMOA platform). A 10-panel cytokine kit was run on 46 blood samples using the SIMOA COREPLEX kit.
- Demographics were compared between LGI1 AE and migraine headache control groups with chi-square/Fisher's exact association tests for categorical variables, and with T-test for continuous variables
- Plasma biomarkers of inflammation and neuronal and glial injury concentrations were logarithmically transformed, and outcomes were analyzed using longitudinal regression
- mRS and MOCA scores were analyzed using longitudinal regression

## Results

**Figure 1: mRS in the LGI1 AE Cohort Over Time of Disease Duration**

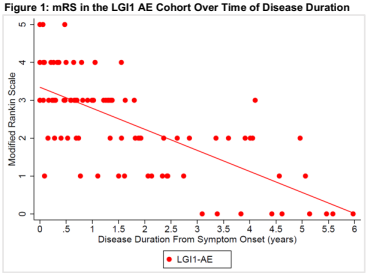



**Figure 2: MoCA in the LGI1 AE Cohort Over Time of Disease Duration**

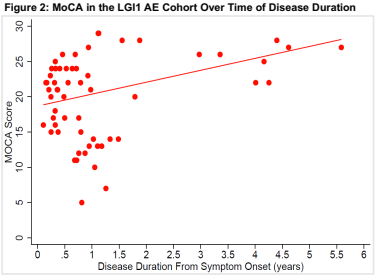



**Figure 3: Plasma NfL LGI1 AE vs. Migraine Headache Controls**

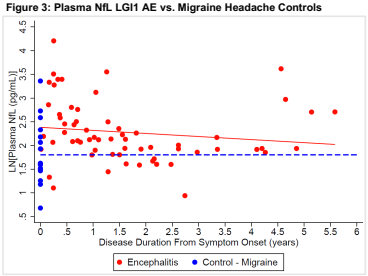



**Figure 4: Plasma GFAP LGI1 AE vs. Migraine Headache Controls**

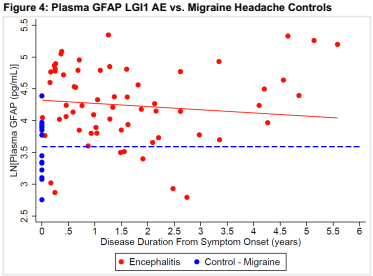



**Figure 5: Cytokine levels (hIL10, hIL6, hIL1b) in LGI1 AE vs. Migraine Headache Controls**

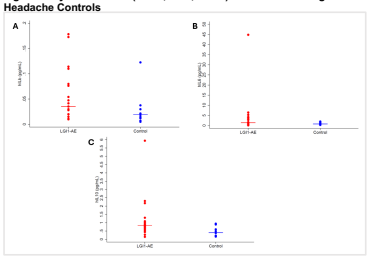
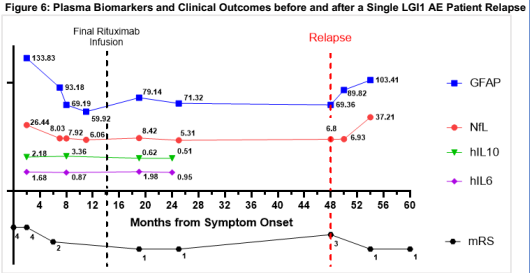



**Figure 6: Plasma Biomarkers and Clinical Outcomes before and after a Single LGI1 AE Patient Relapse**




## Discussion and Conclusions

- mRS scores decrease and MoCA scores increase over time as patients remain on immunotherapy
- This trend of improved mRS and MoCA is paralleled with a decline in NfL and GFAP levels
- After initiation of immune therapy in LGI1 AE patients, there is slow improvement in clinical status over time as reported in previous cohorts, which provides support for the use of NfL and GFAP as markers of disease activity in these patients
- In our cohort, we had one patient relapse, and NfL and GFAP levels increased then declined over time with reimplementation of immunotherapy and improvement of clinical symptoms. This suggests that NfL and GFAP levels may correlate to disease activity
- Multiple cytokines involved in inflammation pathways, including hIL1b, hIL6, and hIL10 were seen to decline over time in patients after implementation of immunotherapy, which provides preliminary data and initial support for further investigation of these cytokines in LG1AE
- Additional systematic studies are needed to better define correlation with disease activity and effects of immunotherapy. It may be helpful to include these blood-based biomarkers as exploratory measures in future randomized controlled trials.
- Limitations of this study include capturing blood-based biomarkers with standard of care clinical visits, introducing variability on the timing of collections The COVID-19 pandemic also led to delays in collections and decreased in person assessments. It is unclear if changes in biomarker levels are reflective of changes in disease activity or are instead an effect of immunotherapy alone. Additionally, we are limited by sample size of 21, acknowledging this is a single center study in a rare disease.

## Disclosures

Amanda L Piquet reports research grants from the University of Colorado, Rocky Mountain MS Center, and the Foundation for Sarcoidosis; consulting fees from Genentech/Roche, UCB, EMD Serono and Alexion; and honorarium from MedLink and publication royalties from Springer as co-editor of a medical textbook.

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