RESEARCH ARTICLE OPEN ACCESS

Risk of Seizure Recurrence Due to Autoimmune Encephalitis With NMDAR, LGI1, CASPR2, and $GABA_BR$ Antibodies

Implications for Return to Driving

Anna Rada, MD, Anne Hagemann, PhD, Charlotte Aaberg Poulsen, PhD, Tobias Baumgartner, MD, Timea Berki, MD, Morten Blaabjerg, MD, PhD, Juliette Brenner, MD, Jeffrey W. Britton, MD, Andrew Christiana, MD, Nicolás L. Ciano-Petersen, MD, Yvette Crijnen, MD, Martin Elišák, MD, Antonio Farina, MD, Alec R. Friedman, MD, Zsófia Hayden, MD, Julien Hébert, MD, MSc, Martin Holtkamp, MD, Zhen Hong, MD, Jerome Honnorat, MD, PhD, Maria Ilyas-Feldmann, MD, PhD, Sarosh R. Irani, BMBCh, MA (Oxon), DPhil, FRCP, FEAN, Stjepana Kovac, MD, Petr Marusic, MD, Sergio Muñiz-Castrillo, MD, PhD, Sudarshini Ramanathan, PhD, Kelsey M. Smith, MD, Claude Steriade, MD, Christine Strippel, MD, Rainer Surges, MD, Maarten J. Titulaer, MD, PhD, Christopher E. Uy, MD, FRCPC, Juna M. de Vries, MD, PhD, Christian G. Bien, MD, and Ulrich Specht, MD

Correspondence
Dr. Rada
anna.rada@mara.de

Neurol Neuroimmunol Neuroinflamm 2024;11:e200225. doi:10.1212/NXI.0000000000200225

Abstract

Background and Objectives

Patients with ongoing seizures are usually not allowed to drive. The prognosis for seizure freedom is favorable in patients with autoimmune encephalitis (AIE) with antibodies against NMDA receptor (NMDAR), leucine-rich glioma-inactivated 1 (LGI1), contactin-associated protein-like 2 (CASPR2), and the gamma-aminobutyric-acid B receptor ($GABA_BR$). We hypothesized that after a seizure-free period of 3 months, patients with AIE have a seizure recurrence risk of <20% during the subsequent 12 months. This would render them eligible for noncommercial driving according to driving regulations in several countries.

Methods

This retrospective multicenter cohort study analyzed follow-up data from patients aged 15 years or older with seizures resulting from NMDAR-, LGI1-, CASPR2-, or $GABA_BR$-AIE, who had been seizure-free for ≥3 months. We used Kaplan-Meier (KM) estimates for the seizure recurrence risk at 12 months for each antibody group and tested for the effects of potential covariates with regression models.

Results

We included 383 patients with NMDAR-, 440 with LGI1-, 114 with CASPR2-, and 44 with $GABA_BR$-AIE from 14 international centers. After being seizure-free for 3 months after an initial seizure period, we calculated the probability of remaining seizure-free for another 12 months (KM estimate) as 0.89 (95% confidence interval [CI] 0.85–0.92) for NMDAR, 0.84 (CI 0.80–0.88) for LGI1, 0.82 (CI 0.75–0.90) for CASPR2, and 0.76 (CI 0.62–0.93) for $GABA_BR$.

From the Department of Epileptology (Krankenhaus Mara) (A.R., C.G.B., U.S.), Medical School, Bielefeld University, Campus Bielefeld-Bethel; Society for Epilepsy Research (A.H.), Bielefeld, Germany; Department of Neurology (C.A.P., M.B.), Odense University Hospital; Department of Clinical Research (M.B.), University of Southern Denmark, Odense, Denmark; Department of Epileptology (T. Baumgartner, R.S.), University Hospital Bonn, Germany; Department of Immunology and Biotechnology (T. Berki), University of Pécs, Medical School, Hungary; Department of Neurology (J.B., Y.C., M.J.T., J.M.V.), Erasmus Medical Center, Rotterdam, Zuid-Holland, the Netherlands; Division of Epilepsy (J.W.B., K.M.S.), Department of Neurology, Mayo Clinic, Rochester, MN; NYU Comprehensive Epilepsy Center (A.C., C. Steriade), New York; French Reference Center on Paraneoplastic Neurological Syndromes and Autoimmune Encephalitis (N.L.C.-P., A.F., J. Honnorat, S.M.-C.), Hospices Civils de Lyon, Hôpital Neurologique, UMR MELIS Inserm 1314 / CNRS 5284, Université Claude Bernard Lyon1, France; Department of Neurology (M.E., P.M.), Second Faculty of Medicine, Charles University, Motol University Hospital, Prague, Czech Republic; Department of Neurology (A.R.F., J. Hébert), Columbia University Irving Medical Center (CUIMC)/New York Presbyterian Hospital, New York; Department of Neurology (Z. Hayden), Medical School, University of Pécs, Pécs, Hungary; Division of Neurology (J. Hébert), University of Toronto, Ontario, Canada; Epilepsy-Center Berlin-Brandenburg (M.H., M.I.-F.), Department of Neurology, Charité - Universitätsmedizin Berlin, Germany; Department of Neurology (Z. Hong), West China Hospital, Sichuan University, Chengdu, China; Oxford Autoimmune Neurology Group (S.R.I., S.R., C.E.U.), Nuffield Department of Clinical Neurosciences, Oxford, United Kingdom; Department of Neurology and Neurosciences (S.R.I.), Mayo Clinic, Jacksonville, FL; Department of Neurology with Institute of Translational Neurology (S.K., C. Strippel), University Hospital Münster, Germany; Translational Neuroimmunology Group (S.R.), Kids Neuroscience Centre, Children's Hospital at Westmead; Faculty of Medicine and Health, University of Sydney; Department of Neurology, Concord Hospital, Sydney, Australia; Division of Neurology (C.E.U.), Department of Medicine, University of British Columbia, Vancouver, Canada; and Laboratory Krone (C.G.B.), Bad Salzuflen, Germany.

Go to Neurology.org/NN for full disclosures. Funding information is provided at the end of the article.

The Article Processing Charge was funded by the authors.

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives License 4.0 (CC BY-NC-ND), which permits downloading and sharing the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Copyright © 2024 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American Academy of Neurology.

Downloaded from https://www.neurology.org by 188.64.37.199 on 6 November 2025

Glossary

AIE = autoimmune encephalitis; **ASM** = antiseizure medication; **CASPR2** = contactin-associated protein-like 2; **CI** = confidence intervals; **COSY** = chance of an occurrence of a seizure in the next year; **DVLA** = Driver and Vehicle Licensing Agency; **FU** = follow-up; **$GABA_BR$** = gamma-aminobutyric-acid B receptor; **KM** = Kaplan-Meier; **LGI1** = leucine-rich glioma-inactivated 1; **NMDAR** = N-methyl-d-aspartate receptor; **ReR** = recurrence risk.

Discussion

Taking a <20% recurrence risk within 12 months as sufficient, patients with NMDAR-AIE and LGI1-AIE could be considered eligible for noncommercial driving after having been seizure-free for 3 months.

Introduction

Losing the ability to drive is one of the most influential consequences for patients with newly diagnosed epileptic seizures.[1] The prognosis for seizure remission is very good in patients with the commonest autoimmune encephalitides (AIEs), caused by cell surface antibodies against the N-methyl-D-aspartate receptor (NMDAR), leucine-rich glioma-inactivated protein 1 (LGI1), contactin-associated protein-like 2 (CASPR2), and the gamma-amino-butyric B receptor ($GABA_BR$).[2,3] However, most patients have recurrent seizures in the acute phase of AIE. In contrast to restrictions related to single acute symptomatic seizures, whereafter patients can return to driving after 3–6 seizure-free months or even without a driving ban[4-6] irrespective of their etiology, driving regulations may view recurrent seizures as "epilepsy" and lead to a driving ban ranging from individually determined intervals to 3 months to 1–2 years.[6]

Reviewing current data on street accident risks of seizures, a European Union expert panel determined that a seizure recurrence risk (ReR) of less than 20%–40% for the following year (a metric they termed chance of an occurrence of a seizure in the next year [COSY]) would allow a safe return to noncommercial driving (group 1 licenses).[7] This risk-based approach formed the basis for the current European directive[8] and has been used in several international publications on driving issues.[9-13] In the United Kingdom, the acceptable risk was adopted and set to a cutoff of 20% by the neurology panel of the Driver and Vehicle Licensing Agency (DVLA).[9]

Systematic, longer-term data on ReR of patients with NMDAR-, LGI1-, CASPR2-, or $GABA_BR$-AIE, who are seizure-free following resolution of the initial illness, are scarce.[2,14-16] Few studies have reported on the duration of seizure freedom in patients suffering from AIE associated with LGI1 and NMDAR antibodies.[2,16] To establish a best estimate of ReR, we collected a multicenter cohort of AIE and performed a pooled analysis of individual patient data. We hypothesized that the seizure ReR in patients with seizures in the context of AIE associated with antibodies against the most frequent extracellular targets (NMDAR, LGI1, CASPR2, and $GABA_BR$) is low enough to support limiting the seizure-free driving ban to 3 months. This would bring the driving restriction in line with the 3-month ban currently imposed on persons following a single acute symptomatic seizure, e.g., in Germany and Switzerland.[6]

Methods

We performed a retrospective multicenter cohort study. Between February and September 2021, we invited research groups worldwide known for their expertise in the field of AIE to share pseudonymized original patient data for a pooled analysis. In addition, we asked all collaborating centers for information on other centers with expertise in AIE. We sent a second request to nonresponders 3 months later. Eleven of 14 centers (including our center) agreed to participate. We were able to recruit 3 additional centers through a recommendation from the centers invited in the first round.

We asked each center to retrospectively identify cases with NMDAR-, LGI1-, CASPR2-, or $GABA_BR$-AIE who fulfilled the following inclusion criteria:

- age 15 years or older at disease onset,
- 1 or more epileptic seizures, and
- seizure freedom for at least 3 months at any point during the disease course.

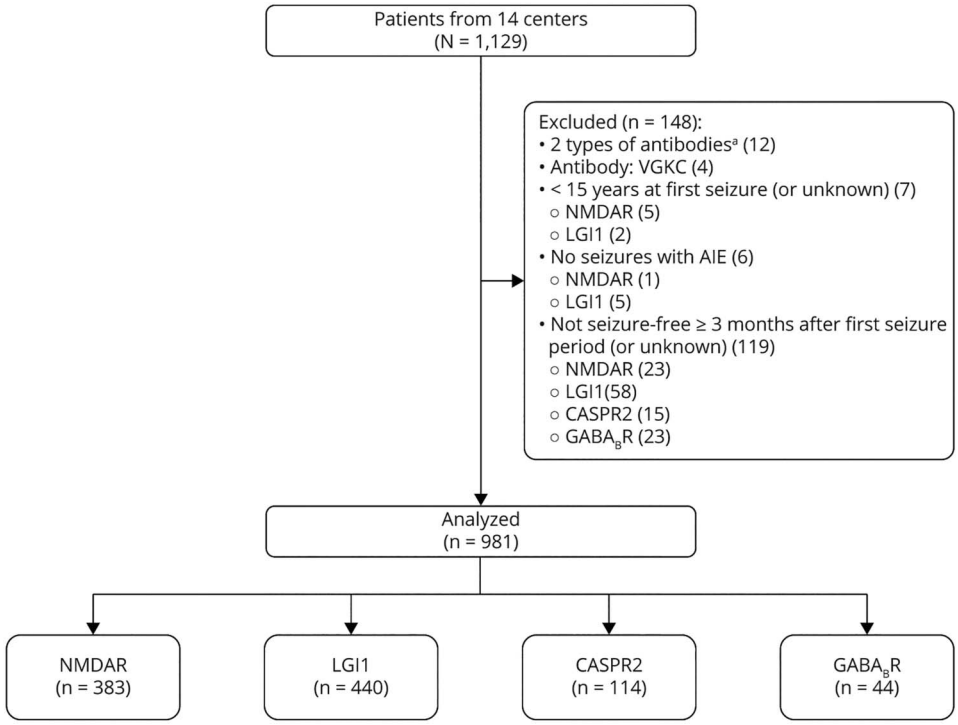
Because of an expected small sample size, AIE due to other antibodies (e.g., $GABA\text{-}_AR$, mGluR-5, or AMPA-R) were not included.[17]

We chose 15 years of age as the lower limit, as by the age of 16, after 12 months of follow-up (FU), patients would be eligible for a noncommercial (group 1) driving license in some US states and several countries worldwide.[18]

For each patient, the following variables were obtained: antibody type; age at first seizure; the duration of up to 4 individual seizure periods; and the time to recurrence after each seizure

Downloaded from https://www.neurology.org by 188.64.37.199 on 6 November 2025

Figure 1 Flow Diagram of Included and Excluded Patients and Reasons for Exclusion



[a]n = 10 with LGI1 and CASPR2 antibodies; n = 1 with NMDAR and α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPAR) antibodies; n = 1 with NMDAR and anti-myelin oligodendrocyte glycoprotein (MOG) antibodies. VGKC = voltage-gated potassium channel, without being able to specify further.

period or, in case of seizure freedom, to last FU (last contact with the patient). Each seizure period was defined by the date of the first seizure of the respective period and, if at least 3 months of seizure freedom had been achieved, by the date of the last seizure. If a patient did not reach ≥3 months seizure freedom, the respective seizure period was defined as ongoing.

We asked the centers to include all seizure types including focal aware seizures, although driving regulations sometimes allow patients with focal aware nondisabling seizures to drive. We did not review seizure data received from the collaborating centers because they all are experts in the field of AIEs and seizures. For the same reason, we did not consider the type of immunotherapy, assuming that all centers follow current therapeutic standards in AIE. Antiseizure medication (ASM) was not considered because there are no standardized recommendations for its use.

The current data on the prognostic relevance of interictal epileptiform potentials in the EEG of patients with AIE with respect to recurrence risk for acute symptomatic seizures are inconclusive; therefore, we did not include this parameter in our consideration.[16,19-22]

Data Analysis

The outcome variable for this study was the time to seizure recurrence, after experiencing 3 months of seizure freedom, the period we determined to be relevant to current driving regulations. We used this variable to estimate the COSY (the probability of a seizure recurrence within the next 12 months) and set the zero point of the time scale to 3 months after the last seizure of a seizure period. This means that patients who are still seizure-free at 12 months on this time scale have not had a seizure for a total of 15 months (3 + 12).

We used the Kaplan-Meier (KM) method to estimate survival curves with 95% CIs.[23] This method takes into account that

Table 1 Sex and Age at First Seizure and the Follow-Up Time for Each Antibody for All Included Patients

	NMDAR	LGI1	CASPR2	GABA$_B$R
N	383	440	114	44
Female, n (%)	313 (81.7%)	151 (34.3%)	5 (4.4%)	19 (43.2%)
Age at first seizure, y				
Mean (SD)	28.0 (13.3)	63.2 (11.6)	64.4 (10.2)	63.6 (11.4)
Median	23.5	65.0	66.1	64.4
Range	15.0–84.2	24.8–92.6	15.4–82.2	31.6–85.1
Follow-up (mo)[a]				
Median	33.1	29.7	37.1	13.6
Range	3.2–214.2	3.0–167.1	3.8–108.1	3.8–100.6

Abbreviations: mo = months; y = year.
[a] Time from end of the first seizure period to the last follow-up.

Downloaded from https://www.neurology.org by 188.64.37.199 on 6 November 2025

Table 2 Numbers of Patients per Seizure Period, Antibody, and Last Observed Outcome for Each Period and at Last Follow-Up

	NMDAR		LGI1		CASPR2		$GABA_BR$	
First seizure period	383		440		114		44	
Seizure-free to last FU	311	81.2%	319	72.5%	82	71.9%	35	79.5%
Recurrence after ≥3 mo[a]	72	18.8%	121	27.5%	32	28.1%	9	20.5%
Second seizure period	72		121		32		9	
<3 mo seizure-free to last FU[b]	10	13.9%	27	22.3%	8	25.0%	3	33.3%
Seizure-free to last FU	44	61.1%	73	60.3%	11	34.4%	4	44.4%
Recurrence after ≥3 mo[a]	18	25.0%	21	17.4%	13[c]	40.6%	2	22.2%
Third seizure period	18		21		13		2	
<3 mo seizure-free to last FU[b]	3	16.7%	8	38.1%	6	46.2%	1	50.0%
Seizure-free to last FU	10	55.5%	11	52.4%	6	46.2%	1	50.0%
Recurrence after ≥3 mo[a]	5	27.8%	2	9.5%	1	7.7%		
Fourth seizure period	5		2		1			
<3 mo seizure-free to last FU[b]	1	10.0%	1	50.0%	1	100%		
Seizure-free to last FU	4	80.0%	1	50.0%				
Outcome at last FU (after last seizure period)	383		440		114		44	
Seizure-free to last FU	369	96.3%	404	91.8%	99	86.8%	40	90.9%
<3 mo seizure-free to last FU[b]	14	3.7%	36	8.2%	15	13.2%	4	9.1%

Abbreviation: FU = follow-up; mo = months.
Note. The numbers and percentages represent the last available outcome for each seizure period. The times to recurrence or last follow-up (FU) vary from patient to patient.
[a] Patients who had become seizure-free for at least 3 mo after a seizure period and then have had a recurrence.
[b] This group includes patients with ongoing seizures and those with <3 mo between the last seizure of this seizure period and the last FU.
[c] For one of these patients, the date of the last seizure of the second seizure period is missing. This patient had a recurrence (i.e., entered a third seizure period) 20 mo after the first recurrence and did not become seizure-free until the last FU.

not all patients experience an event (here: a seizure relapse) in the observation time ("censored data") but uses each patient's data as long as information is available. Each patient is considered as "at risk" to experience the event as long as there is follow-up. We performed separate analyses for the different antibody groups (NMDAR, LGI1, CASPR2, and $GABA_BR$) and seizure periods because more than two-thirds of the patients had only 1 seizure period within the observation time. Patients with more than 1 seizure period were therefore included in several analyses.

In addition, we used regression models to test the effects of potential covariates (sex, age at first seizure, and duration of first seizure period) on the time to seizure recurrence. We tested age at first seizure as a continuous variable and categorized patients into age groups to detect nonlinear effects. Because of the multicenter approach of this study, we used shared frailty models to account for possible heterogeneity between the centers.[24] These models extend the Cox proportional hazard model by introducing a random intercept which allows the baseline hazard to vary between centers.

We used SPSS Statistics (v27) and R software (version 4.2.0), specifically the packages "survival," "survminer," and "coxme."

Standard Protocol Approvals, Registrations, and Patient Consents

The study was approved by the Ethics Committee of the University of Münster, Germany (2018–436-f-S). Because data from the authors' own clinical practice were analyzed, patient consent was waived.

Data Availability

Anonymized data not published within this article will be made available by request from any qualified investigator.

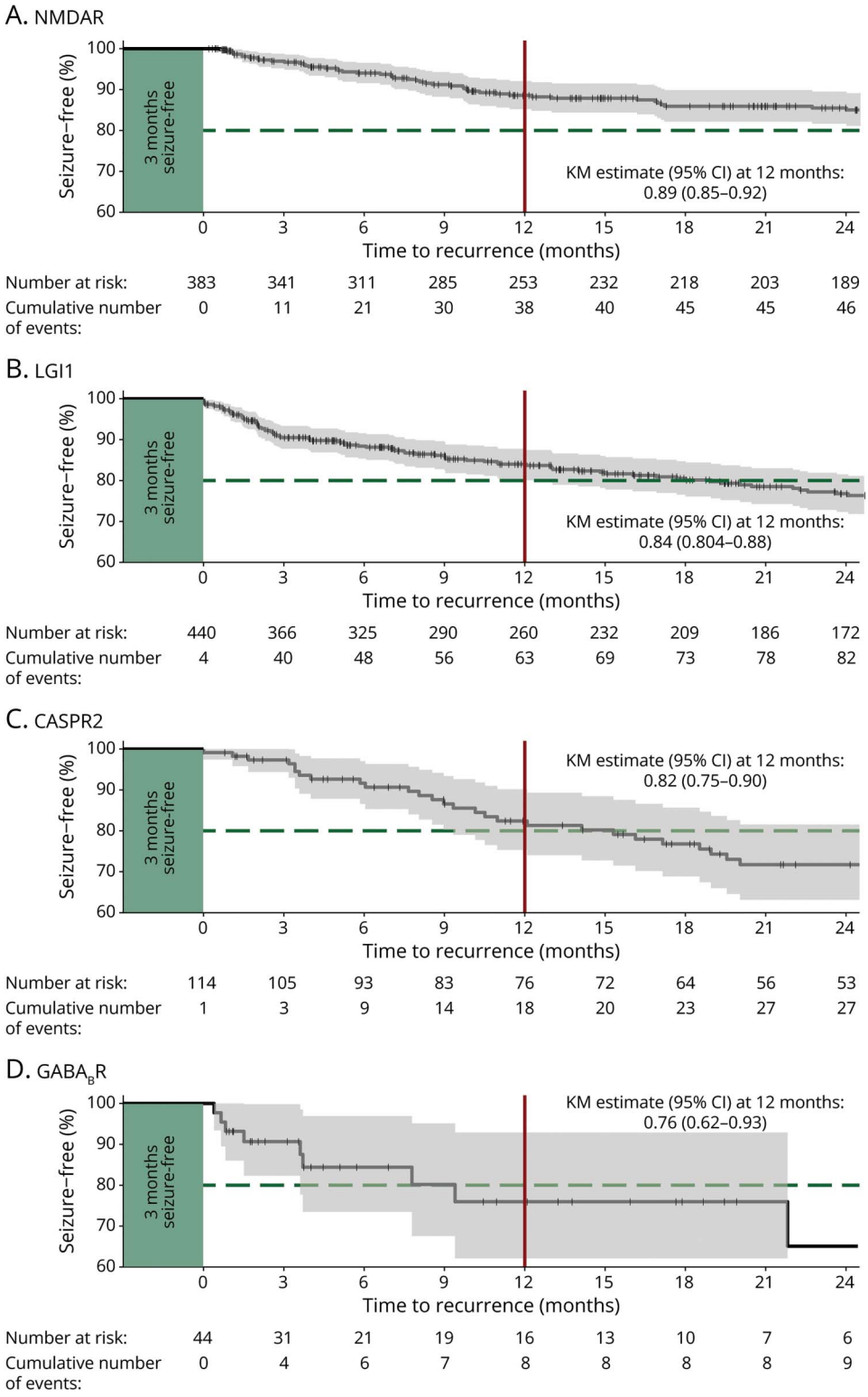
Results

Patient Cohort

In total, 1,129 patients were retrospectively identified from 14 different international centers (n = 17–284 per center). One hundred forty-eight patients were excluded, the most common reason for which was lack of a minimum of seizure freedom for at least 3 months (n = 119/148, 80.4%), leaving

Downloaded from https://www.neurology.org by 188.64.37.199 on 6 November 2025

Figure 2 Survival Curve of Seizure-Free Patients After the First Seizure Period



Kaplan-Meier (KM) estimates (95% confidence interval) for time to seizure recurrence (in months) after being seizure-free for 3 months in the first seizure period in patients with (A) NMDAR, (B) LGI1, (C) CASPR2, and (D) GABA$_B$R antibodies. The dashed green line indicates a seizure recurrence risk of 20%, and the solid red line marks the chance of an occurrence of a seizure in the next year (COSY) 12 months after a 3-month seizure-free period. Abbreviation: cum., cumulative.

981 patients eligible for analysis (Figure 1). Most of these patients had antibodies against NMDAR (n = 383, 39.0%) or LGI1 (n = 440, 44.9%). The patients with NMDAR-AIE were on average younger and more often female than the other 3 groups (both $p < 0.001$, Table 1). The median observation time across all patients was 30.7 months from the last seizure of the first seizure period to the last FU (interquartile range: 14.1–58.8 months, range: 3.0–214.2 months). More than 70%

Downloaded from https://www.neurology.org by 188.64.37.199 on 6 November 2025

Table 3 Kaplan-Meier Estimates (95% CIs) for Being Seizure-Free at 12 Months for Each Seizure Period (Only if n ≥ 10)

	NMDAR	LGI1	CASPR2	$GABA_BR$
First seizure period	0.89 (0.85–0.92) [n = 383]	0.84 (0.804–0.88) [n = 440]	0.82 (0.75–0.90) [n = 114]	0.76 (0.62–0.93) [n = 44]
Second seizure period	0.78 (0.68–0.90) [n = 62]	0.87 (0.80–0.95) [n = 94]	0.62 (0.44–0.87) [n = 23]	[n = 6]
Third seizure period	0.87 (0.71–1.00) [n = 15]	0.83 (0.58–1.00) [n = 13]	[n = 7]	[n = 1]

The sample size (n) for each seizure period denotes the number of patients becoming seizure-free for at least 3 mo after the respective seizure period (i.e., the number at risk at 0 mo as shown in Figure 2 for the first seizure period).

of the patients had only 1 seizure period, that is, they had remained seizure-free to the last FU (Table 2).

NMDAR Antibodies

Figure 2A shows the survival curve of seizure-free patients after a first seizure period with NMDAR-AIE (n = 383), limited to the first 24 months after the required 3-month seizure-free interval. The probability of being seizure-free at 12 months was 0.89 (95% CI 0.85–0.92), resulting in an ReR of 0.11 (95% CI 0.08–0.15). Even at 24 months, the seizure-free rate was >80% (0.86, 95% CI 0.82–0.90). Most patients who experienced a seizure recurrence again achieved another 3-month seizure-free period (62/72, 86.1%, Table 2), but their KM estimate at 12 months was lower (Table 3), resulting in a ReR >20%. The number of patients entering a third or fourth seizure period was low. They mostly became seizure-free (third period: 15/18, 83.3%; fourth period: 4/5, 80.0%, Table 2), and their ReR was low (after the third seizure period, see Table 3). At the end of follow-up, 96.3% of all included patients with NMDAR-AIE were seizure-free (for ≥3 months) after up to 4 seizure periods (Table 2). The regression models showed that neither sex nor age at first seizure or duration of the first seizure period influenced the ReR after the first seizure period (Table 4). For the other seizure periods, the group sizes were too small for subgroup analyses.

LGI1 Antibodies

The survival curve for patients with LGI1-AIE (n = 440) after the first seizure period (Figure 2B) shows that their COSY was just below the cutoff of 20% (ReR at 12 months: 1–0.84 = 0.16, 95% CI 0.12–0.196). This held true for patients who had become seizure-free after a second seizure period (Table 3). Only 2 of 13 patients (15.4%, Table 2) had had a recurrence after a third seizure period (10 and 23 months after the 3-month seizure-free interval), and the only patient who was followed up for >3 months after a fourth seizure period remained seizure-free for at least 2 years (last FU). After up to 4 seizure periods, 91.8% of all patients with LGI1-AIE were seizure-free to last FU (Table 2).

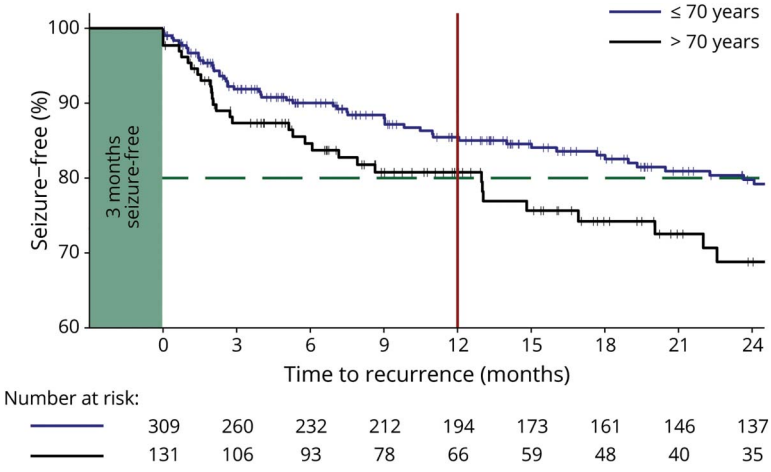
Table 4 Results of Univariable Regression Models (Shared Frailty Models) to Predict Seizure Recurrence After the First Seizure Period

	NMDAR (n = 383)[a]	LGI1 (n = 440)[b]	CASPR2 (n = 114)[c]
Model	**HR (95% CI) *p* Value**	**HR (95% CI) *p* Value**	**HR (95% CI) *p* Value**
A: Sex (male)	1.02 (0.54–1.93) $p = 0.949$	1.03 (0.70–1.52) $p = 0.873$	e
B: Age at first seizure (y)	1.00 (0.98–1.02)[d] $p = 0.849$	1.01 (0.99–1.03) $p = 0.358$	1.03 (0.98–1.07) $p = 0.244$
C: Age group at first seizure	Ref. ≤20 y	Ref. ≤60 y	Ref. ≤65 y
	>20–30 y 0.70 (0.41–1.22) $p = 0.212$	>60–70 y 1.10 (0.71–1.71) $p = 0.657$	>65 y 0.95 (0.46–1.94) $p = 0.883$
	>30 y 0.86 (0.48–1.53) $p = 0.420$	>70 y 1.66 (1.04–2.63) $p = 0.032$	
D: Duration of first seizure period (d)	1.00 (0.999–1.001) $p = 0.817$	1.00 (0.999–1.000) $p = 0.193$	1.00 (0.999–1.001) $p = 0.851$

Abbreviations: d = days; HR = hazard ratio; Ref. = reference category; y = years.
All models include a random intercept for center. For $GABA_BR$, the sample size was too small for reliable regression analysis (n = 44).
[a] Heterogeneity between centers: the range of relative risks between centers varies between 0.80–1.13 (models A and C) and 0.79–1.13 (models B and D).
[b] Heterogeneity between centers: the range of relative risks between centers varies between 0.64–1.46 (model B) and 0.58–1.60 (model D).
[c] Heterogeneity between centers: the range of relative risks between centers varies between 0.68–1.28 (model C) and 0.58–1.32 (model B).
[d] Proportional hazards assumption not met for "age at first seizure" as a continuous variable.
[e] Not done due to the small number of female patients (n = 5/114, 4%).

Downloaded from https://www.neurology.org by 188.64.37.199 on 6 November 2025

Figure 3 Survival Curves of Seizure-Free Patients With LGI1 Antibodies After a First Seizure Period Stratified by Age Group



Kaplan-Meier estimates (95% CI) for time to seizure recurrence (in months) after being seizure-free for 3 months in the first seizure period. The dashed green line indicates a seizure recurrence risk of 20%, and the solid red line marks the chance of an occurrence of a seizure in the next year (COSY) 12 months after a 3-month seizure-free period.

While sex and duration of the first seizure period did not correlate with the ReR (Table 4), seizure recurrence after a first seizure period with LGI1-AIE was related to the age at first seizure: patients aged older than 70 years (n = 131) had a ReR 1.66 times (HR, 95% CI 1.04–2.63) that of patients aged 60 years or younger (n = 156). Patients aged between 61 and 70 years (n = 153) did not differ from those aged 60 years or younger (Table 4). Figure 3 shows survival curves for LGI1 patients stratified by age groups. The KM estimates for seizure freedom at 12 months (after the 3-month seizure-free interval) was slightly lower for patients aged older than 70 years at first seizure (0.81, 95% CI 0.74–0.88) than for patients aged 70 years or younger (0.85, 95% CI 0.81–0.90).

CASPR2 and $GABA_BR$ Antibodies

For CASPR2 (n = 114) and $GABA_BR$ (n = 44), the COSY after first seizure period as estimated with the KM method was >20% (95% CI for seizure freedom at 12 months cross the 0.80 lines in Figure 2, C and D). Although the KM estimate for CASPR2 is just above 0.80, it is below this value for $GABA_BR$ (Table 3). Cox regression models did not show an influence of age at first seizure or duration of the first seizure period on the seizure recurrence after a first seizure period with CASPR2-AIE (Table 4). We did not test the effect of patient sex with Cox regression due to the small number of female patients with CASPR2 (Table 1), but only 1 of 5 women had a recurrence within the observation time (4 months after the 3-month seizure-free period). For $GABA_BR$, the group size was too small for reliable regression analysis. The outcomes for the subsequent seizure periods are summarized in Tables 2 and 3.

Discussion

With this multicenter study, we calculated the seizure ReR for different types of AIE after a predefined seizure-free period of 3 months. Our cohort showed high rates of patients who were seizure-free to last follow-up, ranging from 71.9% (CASPR2-AIE) to 81.2% (NMDAR-AIE) after a first seizure period and are in line with previous findings from smaller cohorts. The same holds true for the age at onset and sex distribution in the different antibody groups.[2,3,25,26]

After achievement of an initial 3-month seizure-free period, the probability for seizure recurrence for the following year (COSY) was <20% for NMDAR-AIE (89% of patients were seizure-free after 1 year), LGI1-AIE (83.8%), and CASPR2-AIE (82.4%). The 95% CI in the CASPR2-AIE cohort did not exclude a 20% ReR (75.3–90.2); however, the group size was considerably smaller than for the NMDAR- and LGI1-AIE cohorts. The $GABA_BR$-AIE cohort estimate (76%) failed to reach the 20% limit. Previous studies have not provided all the information required to estimate the COSY.[2,14-16,27,28]

Seizure remission rates were somewhat lower in patients who had experienced a seizure recurrence after being seizure-free for at least 3 months. However, in this group, the probability of still being seizure-free at 1 year after achievement of a new 3-month seizure-free interval was 78% (NMDAR), 87% (LGI1), and 62% (CASPR2). The number of included patients in the second seizure periods was too small for further analyses.

We found no influence of age or sex on seizure ReR, except for a relatively worse prognosis in the group of patients with LG1-AIE older than 70 years. The reason for this result might be due to different therapeutic approaches in this age group; however, we did not consider any type of therapy in this study (see limitations). Another reason could be a different natural history of a LGI1-AIE in that age group or other comorbidities that might influence the course of the disease.

Downloaded from https://www.neurology.org by 188.64.37.199 on 6 November 2025

Seizures occurring during the acute phase of AIE with antibodies against cell surface antigens (such as NMDAR, LGI1, CASPR2, and $GABA_BR$) have recently been described to follow the concept of acute symptomatic seizures[29] instead of seizures due to autoimmune epilepsy which are regarded as unprovoked allowing for the diagnosis of epilepsy.[2,3,15,25] Our data support this view, confirming high rates of terminal seizure remission.

Driving restrictions may have major consequences on a patient's educational, professional, and social life. The challenge for driving authorities is to balance the risks of seizure-related accidents for the community and limitations in social participation for the individual with seizures. Defining a threshold value for ReR based on data on general traffic risks provides the opportunity for a more individualized assessment of driving eligibility.[7,12] Taking the 20% limit (including the 95% CI) set by the DVLA[9] as a conservative approach, our data suggest that patients with a first seizure episode as a consequence of AIE due to NMDAR and LGI1 antibodies could be allowed to return to noncommercial driving after being seizure-free for 3 months.

In those driving regulations in which an acute symptomatic seizure leads to a shorter mandatory seizure-free interval compared with epilepsy or to first unprovoked seizures, this exception is limited to a single seizure event.[6,8,30] The rationale for that regulation seems to be an analogy to recurrent unprovoked seizures in patients with seizures of unknown cause or a remote symptomatic structural cause, which carry a higher ReR compared with single seizures.[31] There are insufficient data regarding multiple acute symptomatic seizures, except for acute symptomatic seizures presenting as status epilepticus, which are related to a higher risk of unprovoked seizures.[32] In the acute phase of an AIE with NMDAR, LGI1, CASPR2, or $GABA_BR$ antibodies, recurrent rather than single seizures are the rule, and single seizures seem to be rare.[2,28] In contrast to recurrent unprovoked seizures of structural or unknown origin, our data demonstrate that recurrent seizures caused by AIE due to NMDAR, LGI1, and CASPR2 antibodies carry a more favorable prognosis for remission. We could not extract patients with single seizure from our data. As a surrogate, we tested for a potential effect of the duration of the seizure period on the ReR and did not find a correlation.

We think that our favorable results warrant a 3-month maximal driving ban in these patients similar to that for a (single) acute symptomatic seizure. Only the UK driving guidelines acknowledge the good prognosis of AIE by allowing patients with "acute encephalitic illness … including limbic encephalitis associated with seizures" to drive after 6 months of seizure freedom.[30] Our data provide evidence that may warrant reconsideration of this restriction.

For the selection of centers invited, we did not perform a systematic search of publications describing patient cohorts with AIE. Thus, we might have missed research groups with published data on these entities. Patients treated in specialized centers may represent a selection bias toward more severe cases.

Therapeutic approaches for seizures due to AIE reported in the literature are neither standardized nor uniform, making it difficult to classify and compare treatment regimens.[20,33,34] However, the effect of ASM on seizures in AIE with antibodies against surface antigens seems to be marginal,[2,35,36] with a low risk for seizure recurrence after stopping ASM.[25] Thus, we decided not to consider the therapeutic approaches of the cooperating centers in this study. Therefore, we cannot draw a conclusion on the possible effects of different therapeutic strategies. We even cannot exclude that a small proportion of patients (e.g., with mild seizures only) were not treated at all or refused a long-term maintenance therapy. As a consequence, the ReR might be overestimated. On the other hand, final remission rates might be overestimated because we included only patients who had achieved 3 months of seizure freedom, suggesting a selection of patients with an a priori better prognosis. Thus, our outcome data cannot be compared with results of studies investigating therapy of unselected patients.

We did not assess the types of epileptic seizures. Some driving regulations allow patients with focal aware seizures to drive. However, we did not exclude these seizure types because driving permissions for such seizures usually require an observation period of more than 3 months, are limited to a semiology which does not interfere with driving ability (e.g., no motor or visual symptoms),[4,6,30] and have to be the only seizure type during the whole observation period. In addition, many US state driving regulations still lack such an exception for focal aware seizures.[5]

In addition, we could not provide data to address severity of AIE (e.g., cognitive impairment, psychiatric symptoms, or admission to ICU) factors that might influence seizure outcome after AIE.[37]

We did not capture the number or frequency of seizures and the interval from the first seizure to the start of therapy. A longer delay between the initial AIE symptoms and the start of therapy has been shown to correlate with an unfavorable outcome.[2,36,38-40] However, the duration of the seizure periods did not significantly influence the seizure recurrence risk in our data. In many previous studies on the prognosis of epilepsy and subsequent seizure risk, the number of seizures before seizure freedom could be achieved inversely correlated with seizure burden.[41] Thus, in an individual patient, this low seizure risk may deviate from the risk of the whole cohort.

Seizure freedom was assessed retrospectively by patients' reports only. A prolonged video-EEG monitoring may be useful in a smaller proportion of patients to control for occurrence of unrecognized or unrecalled seizures, as suggested by a recent

Downloaded from https://www.neurology.org by 188.64.37.199 on 6 November 2025

case series in LGI1 and CASPR2 patients.[42] The effect of subclinical seizures identified in this manner on driving safety is unknown at this time; nonetheless, the existence of this phenomenon needs to be kept in mind in rendering final recommendations to patients and authorities. Thus, in individual situations, further evaluation to clarify seizure control may be prudent. This limitation, however, applies to all patients with seizures and epilepsy, regardless of the underlying etiology, and is not common practice for several reasons (availability, recording capacity, and undetermined lengths of programmed EEG monitoring).

Finally, it was not feasible to look at the effect of other potential consequences of AIE such as cognitive outcome that might affect driving safety.[43] Therefore, the importance of this study lies in indicating that a significant proportion of patients with this condition do not warrant seizure-specific driving restrictions given the large number with seizure remission.

By using an international multicenter approach, we collected data from a large cohort of patients with seizures due to AIE against cell surface antigens. This endeavor has provided reliable information on the course of seizures in individual patients. We calculated seizure ReR estimates for the different types of antibodies for up to several years, including the outcomes after seizures had recurred. However, a very few patients had recurrences, so the numbers in the latter groups are small.

Because we have used data from clinical practice, our results could be used by driving experts and authorities to adopt driving regulations. Thus, our findings could be a step toward a more individualized assessment of driving eligibility.

Additional studies could investigate the influence of seizure types and frequency on seizure ReR, as well as the interval between the first seizure or other presenting symptoms and the start of therapy. In addition, more research regarding the type of immunotherapy and the value of ASM in patients with seizures due to AIE is needed.

Study Funding

The authors report no targeted funding.

Disclosure

J. Britton reports an inventor agreement—SEER Medical. J. Hébert received salary support through a grant from the American Epilepsy Society during his work on this project. M. Holtkamp received speaker's honoraria and/or consultancy fees from Angelini, Bial, Desitin, Eisai, Jazz Pharma, neuraxpharm, UCB, and Zogenix with the last 3 years. S.R. Irani has received honoraria from UCB, Immunovant, MedImmun, Roche, Janssen, Cerebral therapeutics, ADC therapeutics, Brain, Medlink Neurology and research support from CSL Behring, Janssen, UCB, and ONO Pharma, and is an inventor on 'Diagnostic Strategy to improve specificity of CASPR2 antibody detection (PCT/G82019/051257) and receives royalties on a licensed patent application for LGI1/CASPR2 testing as coapplicant (PCT/GB2009/051441) entitled 'Neurological Autoimmune Disorders'. P. Marusic have received fees as speaker or for serving on the advisory board from Angelini, Biogen, Egis, Eisai, UCB Pharma. These activities were not related to the content of this manuscript. S. Ramanathan has received research funding from the National Health and Medical Research Council (Australia), the Petre Foundation, the Brain Foundation (Australia), the Royal Australasian College of Physicians, and the University of Sydney. She was supported by an NHMRC Investigator Grant (GNT2008339). She serves as a consultant on an advisory board for UCB and Limbic Neurology, and has been an invited speaker for Biogen, Excemed, and Limbic Neurology. R. Surges has received fees as a speaker or for serving on the advisory board from Angelini, Arvelle, Bial, Desitin, Eisai, Janssen-Cilag GmbH, Livanova, Novartis, Precisis GmbH, UCB Pharma, UnEEG, and Zogenix. These activities were not related to the content of this manuscript. K. Smith receives research support from a grant from CURE Epilepsy. U. Specht is a co-chair of the Driving License Commission of the German Society of Epileptology. He reports no other disclosures. C. Steriade performs consulting for The Epilepsy Study Consortium—salary support given to NYU for work provided to the following entities: Alterity, Baergic, Biogen, BioXcel, Cerebral, Cerevel, Eliem, Equilibre, Janssen, Longboard, Lundbeck, Marinus, NeuCyte, Neurocrine, Neuroelectrics, Ono, SK Life Science, and UCB. She also receives grants from NINDS, NCATS, NORD, UCB, and from Parekh Centre for Interdisciplinary Neurology outside the submitted work. J.M. de Vries, M.J. Titulaer, and J. Honnorat of this publication are members of the European Reference Network for Rare Immunodeficiency, Autoinflammatory and Autoimmune Diseases—Project ID No 739543 (ERN-RITA; HCP Erasmus MC and HCP Lyon). M.J. Titulaer has filed a patent, on behalf of the Erasmus MC, for methods for typing neurological disorders and cancer, and devices for use therein, and has received research funds for serving on a scientific advisory board of Horizon Therapeutics, for consultation at Guidepoint Global LLC, for consultation at UCB, for teaching colleagues at Novartis. MT has received an unrestricted research grant from Euroimmun AG and from CSL Behring. C. Aaberg, J. Brenner, Y. S. Crijnen, T. Baumgartner, T. Berki, C.G. Bien, M. Blaabjerg, N.L. Ciano-Petersen, M. Elisak, A. Farina, A.R. Friedman, A. Hagemann, Z. Hayden, Z. Hong, M. Ilyas-Feldmann, S. Kovac, S. Muñiz-Castrillo, A. Rada, Kelsey M. Smith, C. Strippel, and C. Uy report no disclosures relevant to the manuscript. Go to Neurology.org/NN for full disclosures.

Publication History

Received by *Neurology: Neuroimmunology & Neuroinflammation* October 10, 2023. Accepted in final form February 6, 2024. Submitted and externally peer reviewed. The handling editor was Editor Josep O. Dalmau, MD, PhD, FAAN.

Downloaded from https://www.neurology.org by 188.64.37.199 on 6 November 2025

Appendix Authors

Name	Location	Contribution
Anna Rada, MD	Department of Epileptology (Krankenhaus Mara), Medical School, Bielefeld University, Campus Bielefeld-Bethel, Germany	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; analysis or interpretation of data
Anne Hagemann, PhD	Society for Epilepsy Research, Bielefeld, Germany	Drafting/revision of the manuscript for content, including medical writing for content; analysis or interpretation of data
Charlotte Aaberg Poulsen, PhD	Department of Neurology, Odense University Hospital, Denmark	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Tobias Baumgartner, MD	Department of Epileptology, University Hospital Bonn, Germany	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Timea Berki, MD	Department of Immunology and Biotechnology, University of Pécs, Medical School, Hungary	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Morten Blaabjerg, MD, PhD	Department of Neurology, Odense University Hospital; Department of Clinical Research, University of Southern Denmark, Odense, Denmark	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Juliette Brenner, MD	Department of Neurology, Erasmus Medical Center, Rotterdam, Zuid-Holland, the Netherlands	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Jeffrey W. Britton, MD	Division of Epilepsy, Department of Neurology, Mayo Clinic, Rochester, MN	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Andrew Christiana, MD	NYU Comprehensive Epilepsy Center, New York	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Nicolás L. Ciano-Petersen, MD	French Reference Center on Paraneoplastic Neurological Syndromes and Autoimmune Encephalitis, Hospices Civils de Lyon, Hôpital Neurologique, UMR MELIS Inserm 1314 / CNRS 5284, Université Claude Bernard Lyon1, France	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Yvette Crijnen, MD	Department of Neurology, Erasmus Medical Center, Rotterdam, Zuid-Holland, the Netherlands	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Martin Elišák, MD	Department of Neurology, Second Faculty of Medicine, Charles University, Motol University Hospital, Prague, Czech Republic	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Antonio Farina, MD	French Reference Center on Paraneoplastic Neurological Syndromes and Autoimmune Encephalitis, Hospices Civils de Lyon, Hôpital Neurologique, UMR MELIS Inserm 1314 / CNRS 5284, Université Claude Bernard Lyon1, France	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Alec R. Friedman, MD	Department of Neurology, Columbia University Irving Medical Center (CUIMC)/New York Presbyterian Hospital, New York	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Zsófia Hayden, MD	Department of Neurology, Medical School, University of Pécs, Hungary	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Julien Hébert, MD, MSc	Department of Neurology, Columbia University Irving Medical Center (CUIMC)/New York Presbyterian Hospital, New York; Division of Neurology, University of Toronto, Ontario, Canada	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Martin Holtkamp, MD	Epilepsy-Center Berlin-Brandenburg, Department of Neurology, Charité - Universitätsmedizin Berlin, Germany	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Zhen Hong, MD	Department of Neurology, West China Hospital, Sichuan University, Chengdu, China	Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data
Jerome Honnorat, MD, PhD	French Reference Center on Paraneoplastic Neurological Syndromes and Autoimmune Encephalitis, Hospices Civils de Lyon, Hôpital Neurologique, UMR MELIS Inserm 1314 / CNRS 5284, Université Claude Bernard Lyon1, France	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Maria Ilyas-Feldmann, MD, PhD	Epilepsy-Center Berlin-Brandenburg, Department of Neurology, Charité - Universitätsmedizin Berlin, Germany	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data

Downloaded from https://www.neurology.org by 188.64.37.199 on 6 November 2025

Appendix *(continued)*

Name	Location	Contribution
Sarosh R. Irani, BMBCh, MA (Oxon), DPhil, FRCP, FEAN	Oxford Autoimmune Neurology Group, Nuffield Department of Clinical Neurosciences, Oxford, United Kingdom; Department of Neurology and Neurosciences, Mayo Clinic, Jacksonville, FL	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Stjepana Kovac, MD	Department of Neurology with Institute of Translational Neurology, University Hospital Münster, Germany	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Petr Marusic, MD	Department of Neurology, Second Faculty of Medicine, Charles University, Motol University Hospital, Prague, Czech Republic	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Sergio Muñiz-Castrillo, MD, PhD	French Reference Center on Paraneoplastic Neurological Syndromes and Autoimmune Encephalitis, Hospices Civils de Lyon, Hôpital Neurologique, UMR MELIS Inserm 1314 / CNRS 5284, Université Claude Bernard Lyon1, France	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Sudarshini Ramanathan, PhD	Oxford Autoimmune Neurology Group, Nuffield Department of Clinical Neurosciences, Oxford, United Kingdom; Translational Neuroimmunology Group, Kids Neuroscience Centre, Children's Hospital at Westmead; Faculty of Medicine and Health, University of Sydney; Department of Neurology, Concord Hospital, Sydney, Australia	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Kelsey M. Smith, MD	Division of Epilepsy, Department of Neurology, Mayo Clinic, Rochester, MN	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Claude Steriade, MD	NYU Comprehensive Epilepsy Center, New York	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Christine Strippel, MD	Department of Neurology with Institute of Translational Neurology, University Hospital Münster, Germany	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Rainer Surges, MD	Department of Epileptology, University Hospital Bonn, Germany	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Maarten J. Titulaer, MD, PhD	Department of Neurology, Erasmus Medical Center, Rotterdam, Zuid-Holland, the Netherlands	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Christopher E. Uy, MD, FRCPC	Oxford Autoimmune Neurology Group, Nuffield Department of Clinical Neurosciences, Oxford, United Kingdom; Division of Neurology, Department of Medicine, University of British Columbia, Vancouver, Canada	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Juna M de Vries, MD, PhD	Department of Neurology, Erasmus Medical Center, Rotterdam, Zuid-Holland, the Netherlands	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data
Christian G. Bien, MD	Department of Epileptology (Krankenhaus Mara), Medical School, Bielefeld University, Campus Bielefeld-Bethel; Laboratory Krone, Bad Salzuflen, Germany	Drafting/revision of the manuscript for content, including medical writing for content; study concept or design; analysis or interpretation of data
Ulrich Specht, MD	Department of Epileptology (Krankenhaus Mara), Medical School, Bielefeld University, Campus Bielefeld-Bethel, Germany	Drafting/revision of the manuscript for content, including medical writing for content; study concept or design; analysis or interpretation of data

References

1. Jacoby A, Ring A, Whitehead M, Marson A, Baker GA. Exploring loss and replacement of loss for understanding the impacts of epilepsy onset: a qualitative investigation. *Epilepsy Behav.* 2014;33:59-68. doi:10.1016/j.yebeh.2014.02.015
2. de Bruijn MAAM, van Sonderen A, van Coevorden-Hameete MH, et al. Evaluation of seizure treatment in anti-LGI1, anti-NMDAR, and anti-GABABR encephalitis. *Neurology*. 2019;92(19):e2185-e2196. doi:10.1212/WNL.0000000000007475
3. Steriade C, Britton J, Dale RC, et al. Acute symptomatic seizures secondary to autoimmune encephalitis and autoimmune-associated epilepsy: conceptual definitions. *Epilepsia*. 2020;61(7):1341-1351. doi:10.1111/epi.16571
4. Austroads, National Transport Commission Australia (NTC). *Assessing Fitness to Drive 2022 for Commercial and Private Vehicle Drivers*; 2022. Accessed October 2, 2023. austroads.com.au/publications/assessing-fitness-to-drive/ap-g56
5. Ma BB, Bloch J, Krumholz A, et al. Regulating drivers with epilepsy in Maryland: results of the application of a United States consensus guideline. *Epilepsia*. 2017;58(8):1389-1397. doi:10.1111/epi.13804
6. Möller L, Krämer G, Habermehl L, Menzler K, Knake S. Driving regulations for epilepsy in Europe. *Seizure*. 2023;109:83-91. doi:10.1016/j.seizure.2023.05.016
7. Second European Working Group on Epilepsy and Driving. *Epilepsy and Driving in Europe. A Report of the Second European Working Group on Epilepsy and Driving, an Advisory Board to the Driving Licence Committee of the European Union. Final Report. [online]*. Accessed October 2, 2023. ec.europa.eu/transport/road_safety/system/files/2021-07/epilepsy_and_driving_in_europe_final_report_v2_en.pdf
8. European Union. *Commission Directive 2009/113/EC of 25 August 2009 Amending Directive 2006/126/EC of the European Parliament and of the Council on Driving Licences*; 2009. L 223/231-235. Accessed October 2, 2023. eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:223:0031:0035:EN:PDF
9. Bonnett LJ, Tudur-Smith C, Williamson PR, Marson AG. Risk of recurrence after a first seizure and implications for driving: further analysis of the multicentre study of early Epilepsy and Single Seizures. *BMJ*. 2010;341:c6477. doi:10.1136/bmj.c6477
10. Brown JW, Lawn ND, Lee J, Dunne JW. When is it safe to return to driving following first-ever seizure?. *J Neurol Neurosurg Psychiatry*. 2015;86(1):60-64. doi:10.1136/jnnp-2013-307529

Downloaded from https://www.neurology.org by 188.64.37.199 on 6 November 2025

11. Nishida T, Kawai K, Tachimori H. Risks of seizure with fatal traffic crash at wheel in people with epilepsy. *Seizure*. 2020;76:110-115. doi:10.1016/j.seizure.2020.02.002
12. Specht U, Bien CG. Driving eligibility: implications of studies on seizure recurrence risk. *Acta Neurol Scand*. 2020;142(6):541-544. doi:10.1111/ane.13327
13. Engel J, Fisher RS, Krauss G, Krumholz A, Quigg MS. *Expert Panel Recommendations: Seizure Disorders and Commercial Motor Vehicle Driver Safety. [online]*. fmcsa.dot.gov/sites/fmcsa.dot.gov/files/docs/Seizure-Disorders-MEP-Recommendations-v2-prot.pdf
14. Liu X, Yan B, Wang R, et al. Seizure outcomes in patients with anti-NMDAR encephalitis: a follow-up study. *Epilepsia*. 2017;58(12):2104-2111. doi:10.1111/epi.13929
15. Rada A, Birnbacher R, Gobbi C, et al. Seizures associated with antibodies against cell surface antigens are acute symptomatic and not indicative of epilepsy: insights from long-term data. *J Neurol*. 2021;268(3):1059-1069. doi:10.1007/s00415-020-10250-6
16. Smith KM, Dubey D, Liebo GB, Flanagan EP, Britton JW. Clinical course and features of seizures associated with LGI1-antibody encephalitis. *Neurology*. 2021;97(11):e1141–e1149. doi:10.1212/WNL.0000000000012465
17. Dalmau J, Graus F. Antibody-mediated encephalitis. *N Engl J Med*. 2018;378(9):840-851. doi:10.1056/NEJMra1708712
18. Wikipedia. *List of Minimum Driving Ages*; 2022:24. Accessed December 28, 2022. en.wikipedia.org/w/index.php?title=List_of_minimum_driving_ages&oldid=1129480335
19. Gabilondo I, Saiz A, Galán L, et al. Analysis of relapses in anti-NMDAR encephalitis. *Neurology*. 2011;77(10):996-999. doi:10.1212/WNL.0b013e31822cfc6b
20. Guery D, Cousyn L, Navarro V, et al. Long-term evolution and prognostic factors of epilepsy in limbic encephalitis with LGI1 antibodies. *J Neurol*. 2022;269(9):5061-5069. doi:10.1007/s00415-022-11162-3
21. Liu X, Guo K, Lin J, et al. Long-term seizure outcomes in patients with autoimmune encephalitis: a prospective observational registry study update. *Epilepsia*. 2022;63(7):1812-1821. doi:10.1111/epi.17245
22. Shen CH, Fang GL, Yang F, et al. Seizures and risk of epilepsy in anti-NMDAR, anti-LGI1, and anti-GABABR encephalitis. *Ann Clin Translational Neurol*. 2020;7(8):1392-1399. doi:10.1002/acn3.51137
23. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. *J Am Stat Assoc*. 1958;53(282):457-481. doi:10.2307/2281868
24. Therneau TM, Grambsch PM, Pankratz VS. Penalized survival models and frailty. *J Comput Graph Stat*. 2003;12(1):156-175. doi:10.1198/1061860031365
25. Ilyas-Feldmann M, Prüß H, Holtkamp M. Long-term seizure outcome and antiseizure medication use in autoimmune encephalitis. *Seizure*. 2021;86:138-143. doi:10.1016/j.seizure.2021.02.010
26. van Sonderen A, Arino H, Petit-Pedrol M, et al. The clinical spectrum of Caspr2 antibody-associated disease. *Neurology*. 2016;87(5):521-528. doi:10.1212/WNL.0000000000002917
27. Ariño H, Armangue T, Petit-Pedrol M, et al. Anti-LGI1-associated cognitive impairment: presentation and long-term outcome. *Neurology*. 2016;87(8):759-765. doi:10.1212/WNL.0000000000003009
28. van Sonderen A, Thijs RD, Coenders EC, et al. Anti-LGI1 encephalitis: clinical syndrome and long-term follow-up. *Neurology*. 2016;87(14):1449-1456. doi:10.1212/WNL.0000000000003173
29. Beghi E, Carpio A, Forsgren L, et al. Recommendation for a definition of acute symptomatic seizure. *Epilepsia*. 2010;51(4):671-675. doi:10.1111/j.1528-1167.2009.02285.x
30. GOV.UK. *Guidance: Neurological Disorders: Assessing Fitness to Drive (Plus Appendix B: Epilepsy and Seizure Rules and Further Guidance)*; 2022. Accessed October 2, 2023. gov.uk/guidance/neurological-disorders-assessing-fitness-to-drive
31. Hauser WA, Rich SS, Lee JR-J, Annegers JF, Anderson VE. Risk of recurrent seizures after two unprovoked seizures. *N Engl J Med*. 1998;338(7):429-434. doi:10.1056/NEJM199802123380704
32. Hesdorffer DC, Logroscino G, Cascino G, Annegers JF, Hauser WA. Risk of unprovoked seizure after acute symptomatic seizure: effect of status epilepticus. *Ann Neurol*. 1998;44(6):908-912. doi:10.1002/ana.410440609
33. Bien CG. Management of autoimmune encephalitis. *Curr Opin Neurol*. 2021;34(2):166-171. doi:10.1097/WCO.0000000000000909
34. Ganesh A, Bartolini L, Wesley SF. Worldwide survey of neurologists on approach to autoimmune encephalitis. *Neurol Clin Pract*. 2020;10(2):140-148. doi:10.1212/CPJ.0000000000000701
35. Irani SR, Stagg CJ, Schott JM, et al. Faciobrachial dystonic seizures: the influence of immunotherapy on seizure control and prevention of cognitive impairment in a broadening phenotype. *Brain*. 2013;136(Pt 10):3151-3162. doi:10.1093/brain/awt212
36. Thompson J, Bi M, Murchison AG, et al. The importance of early immunotherapy in patients with faciobrachial dystonic seizures. *Brain*. 2018;141(2):348-356. doi:10.1093/brain/awx323
37. Titulaer MJ, McCracken L, Gabilondo I, et al. Treatment and prognostic factors for long-term outcome in patients with anti-NMDA receptor encephalitis: an observational cohort study. *Lancet Neurol*. 2013;12(2):157-165. doi:10.1016/S1474-4422(12)70310-1
38. Dubey D, Singh J, Britton JW, et al. Predictive models in the diagnosis and treatment of autoimmune epilepsy. *Epilepsia*. 2017;58(7):1181-1189. doi:10.1111/epi.13797
39. Matricardi S, Casciato S, Bozzetti S, et al. Epileptic phenotypes in autoimmune encephalitis: from acute symptomatic seizures to autoimmune-associated epilepsy. *J Neurol Neurosurg Psychiatry*. 2022;93(11):1194-1201. doi:10.1136/jnnp-2022-329195
40. Toledano M, Britton JW, McKeon A, et al. Utility of an immunotherapy trial in evaluating patients with presumed autoimmune epilepsy. *Neurology*. 2014;82(18):1578-1586. doi:10.1212/WNL.0000000000000383
41. Chen Z, Brodie MJ, Liew D, Kwan P. Treatment outcomes in patients with newly diagnosed epilepsy treated with established and new antiepileptic drugs: a 30-year longitudinal cohort study. *JAMA Neurol*. 2018;75(3):279-286. doi:10.1001/jamaneurol.2017.3949
42. Baumgartner T, Pitsch J, Olaciregui-Dague K, et al. Seizure underreporting in LGI1 and CASPR2 antibody encephalitis. *Epilepsia*. 2022;63(9):e100–e105. doi:10.1111/epi.17338
43. Wolfe PL, Lehockey KA. Neuropsychological assessment of driving capacity. *Arch Clin Neuropsychol*. 2016;31(6):517-529. doi:10.1093/arclin/acw050

Downloaded from https://www.neurology.org by 188.64.37.199 on 6 November 2025