




## Letters to the Editor: Published Article

# Response to: Management of Seizures and Epilepsy in Patients with Autoimmune Encephalitis

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### Dear Editor,

We thank Dr Burneo for his interest in our recent publication,<sup>1</sup> as well as for his comments. He correctly notes that these Canadian consensus guidelines focus on the acute management of autoimmune encephalitis, prompt treatment of which may reduce the likelihood of developing irreversible structural injury that causes an enduring seizure predisposition (i.e. autoimmune encephalitis-associated epilepsy, or AEAE). It is for this reason that, while we wholeheartedly agree with its importance as part of ongoing care for patients with autoimmune encephalitis, the long-term management of AEAE is not extensively discussed in our publication. We also fully agree with the importance of considering the availability not only of anti-seizure medications (ASMs) but also other symptomatic and disease-modifying therapies for autoimmune encephalitis in different practice settings around the world; however, this is similarly outside the scope of these Canadian-focused guidelines.

Patients with neural antibodies against extracellular targets (e.g. anti-NMDAR, LGI1, CASPR2, GABA(B)R) frequently attain seizure freedom following adequate immunotherapy, indicating acute symptomatic seizures secondary to autoimmune encephalitis rather than AEAE.<sup>2,3</sup> Dr Burneo raises the important point that, particularly among patients harbouring neural antibodies against intracellular targets (e.g. most high-risk paraneoplastic antibodies, anti-GAD65), a substantial proportion develop AEAE despite adequate immunotherapy.<sup>4,5</sup> While evidence for best ASM selection in such patients is limited, emerging data in antibody-specific cohorts (e.g. for use of cenobamate and clobazam combination in patients with anti-GAD65-associated temporal lobe epilepsy) give hope for a more personalised approach in the future.<sup>6</sup>

We share Dr Burneo's view that, following reasonable exclusion of treatable neuroinflammation that could be contributing to seizure burden, patients with medically refractory AEAE may be considered for epilepsy surgery evaluation. It should be acknowledged, however, that evidence for efficacy of epilepsy surgery in patients with AEAE is limited. Furthermore, there is some data to suggest that, particularly for those with anti-GAD65-associated

temporal lobe epilepsy, outcomes may be worse than expected when compared to other aetiologies.<sup>5,7,8</sup> Counselling on the uncertainty surrounding sustained benefit, as well as setting of realistic expectations, are thus essential to shared decision-making when contemplating epilepsy surgery in a patient with medically refractory AEAE.

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### References

1. Hahn C, Budhram A, Alikhani K, et al. Canadian consensus guidelines for the diagnosis and treatment of autoimmune encephalitis in adults. *Can J Neurol Sci.* 2024;1–21.
2. de Bruijn MAAM, van Sonderen A, van Coevorden-Hameete MH, et al. Evaluation of seizure treatment in anti-LGI1, anti-NMDAR, and anti-GABA. *Neurology.* 2019;92:e2185–e96.
3. 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;63:1812–21.
4. Smith KM, Britton JW, Thakolwiboon S, et al. Seizure characteristics and outcomes in patients with neurological conditions related to high-risk paraneoplastic antibodies. *Epilepsia.* 2023;64:2385–98.
5. Malter MP, Frisch C, Zeitler H, et al. Treatment of immune-mediated temporal lobe epilepsy with GAD antibodies. *Seizure.* 2015;30:57–63.

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6. Serrano-Castro PJ, Rodríguez-Uranga JJ, Cabezudo-García P, et al. Cenobamate and clobazam combination as personalized medicine in autoimmune-associated epilepsy with Anti-Gad65 antibodies. *Neurol Neuroimmunol Neuroinflamm*. 2023;10:e200151.
7. Mäkelä KM, Hietaharju A, Brander A, Peltola J. Clinical management of epilepsy with glutamic acid decarboxylase antibody positivity: the interplay between immunotherapy and anti-epileptic drugs. *Front Neurol*. 2018;9:579.
8. Carreño M, Bien CG, Asadi-Pooya AA, et al. Epilepsy surgery in drug resistant temporal lobe epilepsy associated with neuronal antibodies. *Epilepsy Res*. 2017;129:101–5.