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Perampanel for the treatment of focal pharmacoresistant epilepsy: the “real life” experience of our center.

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Objectives: Perampanel (PER) is a selective non-competitive antagonist of post-synaptic glutammatergic receptor AMPA (Fig. 1), originally approved as an add-on drug in epilepsies with focal-onset seizures with or without evolution to bilateral convulsion, and recently also in those with primary generalized seizures. We report our “real life” experience on the use of PER emerging from an open observational perspective study, aimed to evaluate efficacy and safety of PER as an add-on therapy in focal pharmacoresistant epilepsies. As a secondary issue we wanted to note if there were any differences in the efficacy between structural and likely structural epilepsies.

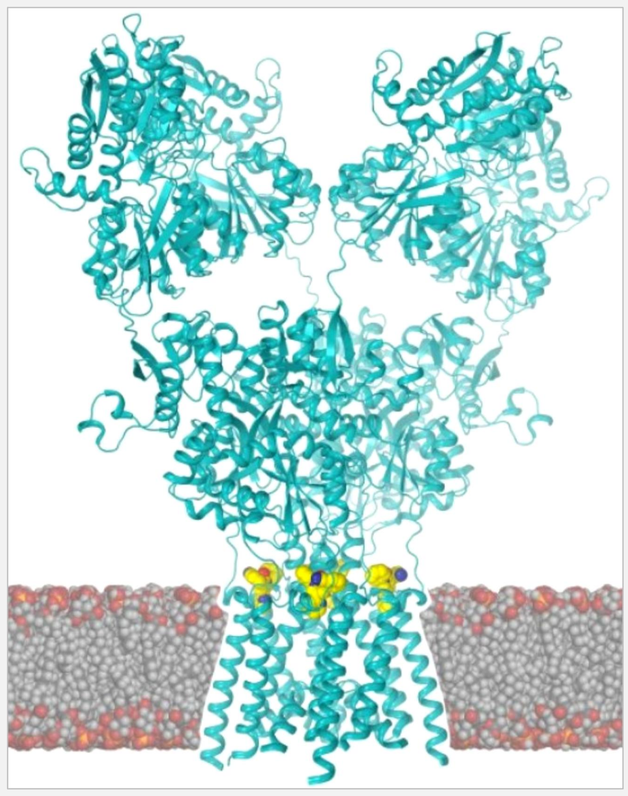

Fig. 1 AMPA receptor (blue) is inactivated by antiepileptic drug Perampanel (yellow), which is wedged into binding saites on the upper edge of the cell membrane (gray and red).
Credit: Laboratory of Alexander Sobolevsky, PhD/Columbia University Medical Center

Materials and Methods: we enrolled, from july 2015 to now, 48 consecutive patients with the diagnosis of focal pharmacoresistant epilepsy (20 F and 28 M, age 17-76 yo), who did not change any therapy in the previous 3 months nore in the following 12 month after the introduction of PER. Of the 48 patients, 29 were suffering from a structural epilepsy (60%, group A) and 19 from a likely structural epilepsy (40%, group B). PER was started at the initial dose of 2 mg/die, with increments of 2 mg/week in 29 patients (60%), already on therapy with CYP3A4 inducers, and of 2 mg/2 weeks in the others until the maximal dose of 12 mg/die. Our goal was to reach a reduction of the seizure frequency ≥ 50%, evaluated through follow-up at 3, 6 or 12 months.

Results: Among the initial 48 patients, 5 haven’t still reached the 3 months follow-up, so that we excluded them from the final evaluation and 3 dropped out within the first 4 weeks for adverse effects (severe dizziness syndrome). So, we considered 40 patients (23 group A and 17 group B): 5 reached the dose of 4 mg, as at upper doses they manifested dizziness syndrome or behavioural disturbances (1 case), while the others reached the lowest tollerated and effective dose (6-12 mg/die). 9 have a 3 months follow-up, 22 a 6 months follow-up and 9 a 12 months follow-up. 20 patients (50% of which 9 belonging to group A and 11 to group B) had a significative reduction of seizure frequency (≥ 50%, responders): 5/9 after 3 months (56%); 11/22 after 6 months (50%), 4/9 after 12 months (44%). 10/48 (21%) suffered from severe dizziness syndrome (3 drop out).

Discussion and conclusions:
Perampanel was effective as an add-on drug in the management of focal pharmacoresistant epilepsies with an acceptable safety profile. Only one patient showed relevant behavioural symptoms, and the commonest adverse effect was dizziness. Patients with “likely structural” epilepsies show to be better responsive to PER, but the small sample doesn’t allow to obtain statistically significative data at this moment.

Main references
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