ADJUNCTIVE PERAMPANEL EFFECTIVENESS AND TOLERABILITY FOR DRUG RESISTANT EPILEPSY IN HONG KONG

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Introduction

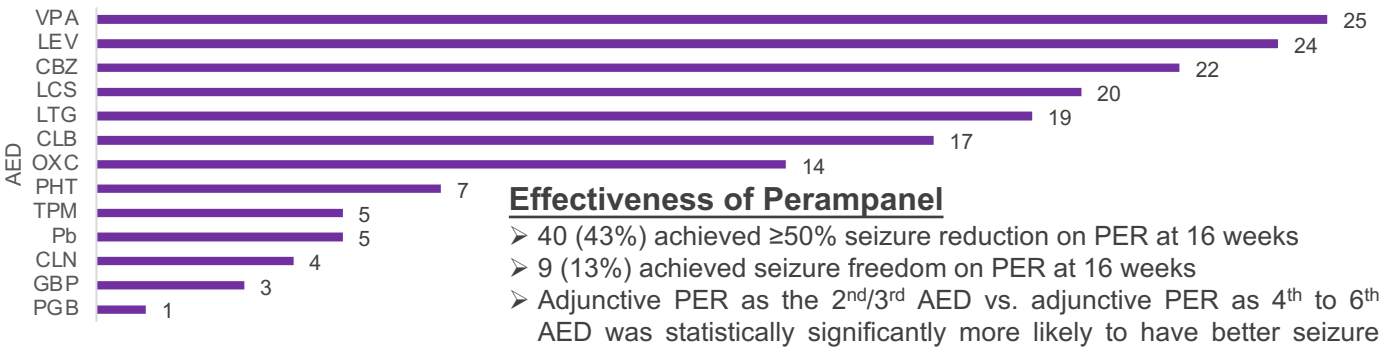
- Drug resistant epilepsy (DRE) is a significant burden for which epilepsy surgery can be an effective option when feasible but not all patients are suitable or willing to undertake the surgical risk
- Anti-epileptic drugs (AEDs) of different mechanisms remain the mainstay of therapy for patients with DRE
- Perampanel (PER) is the 1st orally active non-competitive AMPA receptor antagonist approved for adjunctive therapy in epilepsy
- This study reports effectiveness and tolerability of adjunctive PER in a cohort of DRE patients at PWH in Hong Kong

Methods

- DRE patients attending PWH between July 2016 to June 2021 were prospectively screened and recruited
  - Inclusion : failed ≥2 AEDs before and ≥2 seizures/month
  - Exclusion : psychogenic non-epileptic seizure (PNES)
- Patients were initiated on PER with dosage titrated as deemed appropriate by neurologists at clinic follow up sessions after assessment and completion of the Neuropsychiatric Inventory (NPI) and Zarit Burden Interview (ZBI) at 0 weeks and 16 weeks

Patient Characteristics

- 69 patients (mean age 40, 23-64, 65% female) were recruited and analyzed
- Average PER dose at 16 weeks was 3mg
- Etiologies of epilepsy: 81% structural, 28% genetic, 14% infectious, 3% metabolic, and 12% immune
- Average number of AEDs on starting PER was 2, ranging from 1 to 5
- Below are the number of patients on each concurrent AED



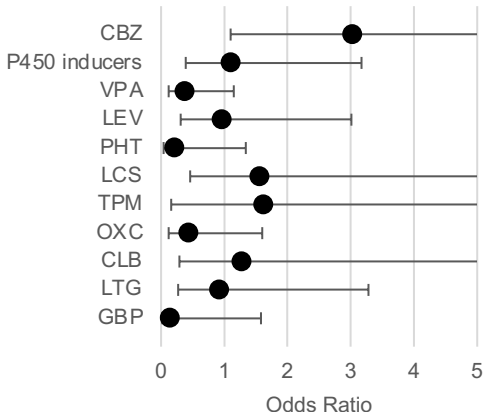
Effectiveness of Perampanel

- 40 (43%) achieved ≥50% seizure reduction on PER at 16 weeks
- 9 (13%) achieved seizure freedom on PER at 16 weeks
- Adjunctive PER as the 2nd/3rd AED vs. adjunctive PER as 4th to 6th AED was statistically significantly more likely to have better seizure control at 16 weeks

Parameter	OR	95% CI	P value
≥50% reduction 2nd/3rd AED vs. 4th-6th	3.20	1.18-8.67	0.020
Seizure freedom 2nd/3rd AED vs. 4th-6th	9.79	1.15-83.12	0.028

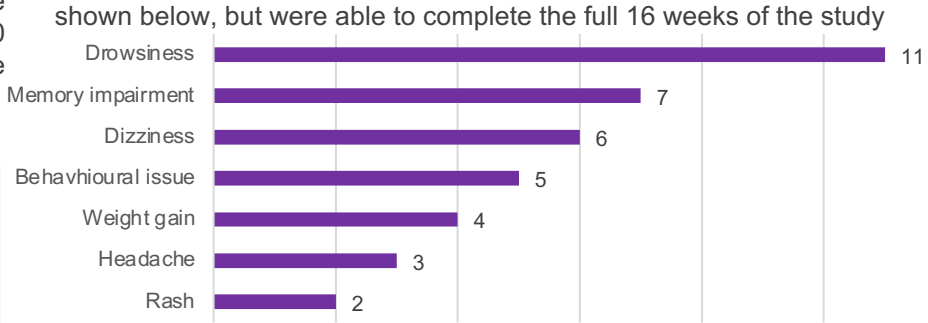
Subgroup Analyses

- No etiology of epilepsy was shown to have better or worse outcomes with PER, including immune related epilepsies
- Concomitant PER and carbamazepine (CBZ) use statistically significantly reduced the odds of >25% seizure reduction raising concerns of P450 related induction with CBZ use causing reduced PER effectiveness
- OR 3.03 (95% CI 1.01-9.10, p=0.044)



Tolerability of Perampanel – TEAE, completed 16 weeks

- 25 (36%) developed treatment emergent adverse effects (TEAEs) as shown below, but were able to complete the full 16 weeks of the study



- GI upset, floaters, blepharospasm, itchiness, cough, lower limbs weakness, facial numbness, and tremor were reported once as well

Tolerability of Perampanel – Withdrawal from Study

- 13 (19%) withdrew from study due to adverse effects before 16 weeks

- Significant behavioural disturbance, memory impairment, dizziness, weight gain, retention of urine, and elevated ALT were reported once as cause of discontinuation
- Otherwise retention rate for adjunctive PER in current study **~80%**
- NPI and ZBI scores at 0 weeks vs. 16 weeks had no statistically significant difference by Mann Whitney U test comparison
  - Entire cohort: NPI: U=1457, **p=0.208**; ZBI: U=2059, **p=0.075**
  - On LEV: NPI: U=196, **p=0.277**; ZBI: U=203, **p=0.162**
- Results indicate a **no significant neuropsychiatric adverse effects** contributed by PER in current cohort, **even in combination with LEV**

Limitations of Study

- Single center study with a small number of patients
- Very few cases of immune epilepsy in this cohort
- Adjunctive PER being more effective when used concomitantly with lower number of AEDs may simply only reflect easier to treat DRE
- PER was previously not available under Hospital Authority (HA) Drug Formulary, limiting the duration of PER to 16 weeks early on in the study, longer term data would be valuable in guiding selection of patients who may benefit more from adjunctive PER

Conclusion

- Adjunctive PER is an effective and generally well tolerated treatment option even in combination with LEV for patients with DRE

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