

## Key message from 1<sup>st</sup> day symposium

**KAMORNWAN KATANYUWONG M.D.**  
**PEDIATRICS DEPARTMENT**  
**CHIANG MAI UNIVERSITY HOSPITAL**

ประชุมวิชาการประจำปีครั้งที่ **18**  
สมาคมโรคลมชักแห่งประเทศไทย

## Update clinical guideline

Dr. Chacrin

### Partial Seizures: Adults Recommendations

Level A: CBZ(n=23), PHT(n=12), LEV(n=1), ZNS(n=1)

Level B: VPA (n=11)

Level C: GBP, LTG, OXC, PB, TPM, VGB

Level D: CZP, PRM

Level E: Others

Level F: None

### Partial Seizures: Children Recommendations

Level A: OXC (no new AEDs)

Level B: None

Level C: CBZ, PB, PHT, TPM, VPA, VGB

Level D: LTG, CLB, CLZ, ZNS

Level E: Others

Level F: None

### Generalized Tonic Clonic Seizures: Adults Recommendations

Level A: None

Level B: None

Level C: CBZ\*,LTG,OXC\*,PB, PHT\*,TPM,VPA

Level D: GBP,VGB

Level E: Others

Level F: None

### Generalized Tonic Clonic Seizures: Children Recommendations

Level A: None

Level B: None

Level C: CBZ\*,PB, PHT\*,TPM,VPA

Level D: OXC\*

### Juvenile Myoclonic Epilepsy : Recommendations

Level A: None

Level B: None

Level C: None

Level D: TPM, VPA

Level E: Others

Level F: CBZ\*, GBP, OXC\*, PHT\*, TGB, VGB

## Prof. Vicente Villanueva

- Practice is the best of all instructors
- No good evidenced-based but clinical-based
- Basis of pharmacoresistant epilepsy are unknown
- Evidence based approach is not enough in the medical treatment strategy
- Rational polytherapy is a suitable option
- Treatment of pharmacoresistant epilepsy is complicated and should be performed among a comprehensive epilepsy program
- Presurgical and surgical strategies are not uniform

### Predictors of pharmaco-resistant epilepsy

Consistent	Inconsistent
Syndrome: symptomatic generalized > nonidiopathic focal > idiopathic	Febrile seizures
High initial seizure frequency	Status epilepticus
Neonatal seizure	EEG discharges or focal slowing
Age at onset >12 years	
Intellectual disability	
Abnormal exam	
Abnormal imaging	
Failure of first AED or failure to respond in first year	<b>EEG : not a biomarker</b>

Wirrell E. *Epilepsia*, 54(Suppl. S2):19-22, 2013

### Pseudo-resistance to AEDs

Reason	Objectives
<b>Wrong diagnosis</b>	Syncope, cardiac arrhythmia, or other conditions; psychogenic nonepileptic seizures → Video-EEG
<b>Wrong drug</b>	Inappropriate for seizure type; pharmacokinetic or pharmacodynamic interactions
<b>Wrong dose</b>	Too low (overreliance on "therapeutic" blood levels); side effects preventing drug increase
<b>Lifestyle issues</b>	-Sleep deprivation -Alcohol and drugs -Hormonal changes -Poor compliance

Kwan P. et al, *N Engl J Med*. 2011;365:919-26  
Faught RE et al, *Epilepsia* 2009;50:501-9

### Rational polytherapy

- Spectrum of activity / MoA
- Favourable interaction
- Minimise adverse event
- Avoid too many drugs

Prof : 2 AEDs  
: some 3 AEDs

Perucca E. *Acta Neurol Scand* 1995;(suppl 162):31-4  
French J & Faught E. *Epilepsia* 2009;50(suppl 8):63-9

### Combinations: Clinical evidence

Combination	Seizure type	n	Reference
LTG + VPA	Several types Partial	347 20	Brodie MJ, et al. <i>Epilepsy Res</i> 1997;26:423-32 Pisani F, et al. <i>Epilepsia</i> 1999;40:1141-6
VPA + ESM	Absences	5	Rowan AJ, et al. <i>Arch Neurol</i> 1983;40:797-802
PHT + PB	GTC, partial Neonatal	41 59	Cereghino JJ, et al. <i>Clin Pharmacol Ther</i> 1975;18:733-41 Painter MJ, et al. <i>N Engl J Med</i> 1999;341:485-9
CBZ + VPA	Partial Partial Partial	107 17 100 18	Brodie MJ & Mumford JP. <i>Epilepsy Res</i> 1999;34:199-205 Walker SA, et al. <i>Epilepsia</i> 1998 (Abstract) Dean JC, et al. <i>Epilepsia</i> 1988;29:140-4 Armour DJ, et al. <i>J Clin Pharm Ther</i> 1988;13:53-64
CBZ + VGB	Partial Partial	108 14	Brodie MJ & Mumford JP. <i>Epilepsy Res</i> 1999;34:199-205 Tanganelli P, et al. <i>Epilepsy Res</i> 1996;25:257-62
VPA + CNZ	Several types	55	Mireles R, et al. <i>Epilepsia</i> 1985;26:122-6
VPA + FBM	Lennox-Gastaut	13	Siegel H, et al. <i>Epilepsy Res</i> 1999;34:91-7
LTG + GBP	Partial	5	Pisani F, et al. <i>Epilepsia</i> 1998 (Abstract)
LTG + VGB	Several types Partial	42 22	Schapel GJ, et al. <i>Seizure</i> 1996;5:51-6 Stolerek I, et al. <i>JNNP</i> 1994; 57: 921-4
LTG + TPM	Several types		
VGB + TGB	Partial		<b>Na blocker with other mechanisms</b>
SCB (+) + multiple MOA	Several types	42	Kwan P & Brodie MJ. <i>Seizure</i> 2000;9:464-8
LCM + SCB (+) or SCB(-)	Partial Partial	158 (104 + 49) 944 (781 + 163)	Vilanova V, et al. <i>Epilepsy Behav</i> 2012;23:298-304 Saxe JS, et al. <i>CNS Drugs</i> 2010;24:1055-6 (post-hoc)

### Newest gen of AED: evidence-based and practical use

Dr Surachai

#### Pediatric use of Lasosamide

- Not yet FDA approve
- However, data of the use of lacosamide in pediatric population is promising **add on partial sz**
  - Use in pediatric patients
  - Use in very young patients
  - Use in Lennox-Gastaut syndrome
  - Use in Status epilepticus

**Rufinamide**

**Adult ≥ 16 yrs**

### Rufinamide

#### Childhood indication

- FDA approve in adjunctive treatment in LGS > 4 yrs of age especially in "Drop attack" (atonic and tonic seizure)
- Other use
  - Infantile spasm (Olsen, *Epilepsy & Behavior*, 2012)
    - 107 patients (17 mo.-23 yrs)
    - Median follow-up 171 day (10-408)
    - Responder rate 53% (median reduction 50%)
    - Side effect 38% (discontinue 18%)
- Focal seizures
- NOT for Dravet syndrome

### Stiripental

- Orphan drug for Dravet syndrome
- Disadvantage
  - Nonlinear pharmacokinetics
  - Potent inhibition of liver cytochrome P450 enzymes
  - High protein binding and drug interaction

Other use : Atypical absence, partial seizure

Optimal use of old and new AEDS Dr. Rungsan

### Key factors on optimal use of AEDs

- Efficacy
- Side effect / Safety / tolerability
- Pharmacology
  - Initiation/dosage
  - Hepatic enzyme induction
  - Drug-drug interaction
- Co-morbidities
- Special groups

Optimal use of old and new AEDS Dr. Rungsan

### Take home message

- Controlling seizures is one of the most important influences on quality of life (QOL).
- Some seizures have little impact on QOL.
- Some drug' adverse effects lower quality of life much more than seizures.
- **Therefore, therapy should aim at QOL, not only seizure control.**

Dr. Kamornwan

### AED regimens with relatively high teratogenicity

- **VPA** > 1,000 mg/day ( some > 1,500 )
- PB > 200 mg/day
- CBZ + VPA
- CBZ+ VPA+ PB+/- PHT
- PB+ PHT + primidone
- Benzodiazepines + other AEDs
- Caffeine + PB+/- other AEDs

Samren et al, Battino et al, Lindout et al, Dansky

Dr. Kamornwan

### Optimal use of old and new AEDS

**TABLE 1. Age effects on pharmacokinetic parameters (compared with adult values)**

	Neonates/Infant	Children	Adults
Renal	↓	↔	↔
Metabolism			
CYP	↓	↑	↔
UGT	↓	↔	↔
Albumin	↓	↔	↔

CYP, cytochrome P450; UGT, uridine diphosphate, glucuronosyl transferase.

Children

- ↑mg/kg/dose, MKD
- Interval of AED

*Epilepsia 2002;43:53-59*

Dr. Montida

### Epileptic VS Non epileptic

- NFLE VS. PNES
- Cataplexy ... transient episode of muscle weakness but full conscious awareness
  - ....excessive daytime sleepiness
  - .. triggered by emotion