VII CONGRESSO NAZIONALE ANEU 2022
Roma – 30 Settembre

Controversie in Neurologia

Come trattare lo stato epilettico? Con vecchi farmaci

C. Di Bonaventura

Outline

- Status Epilepticus
  - > Operational definitions
  - > Basic principles of treatment
  - > Role of old ASMs

Operational definitions

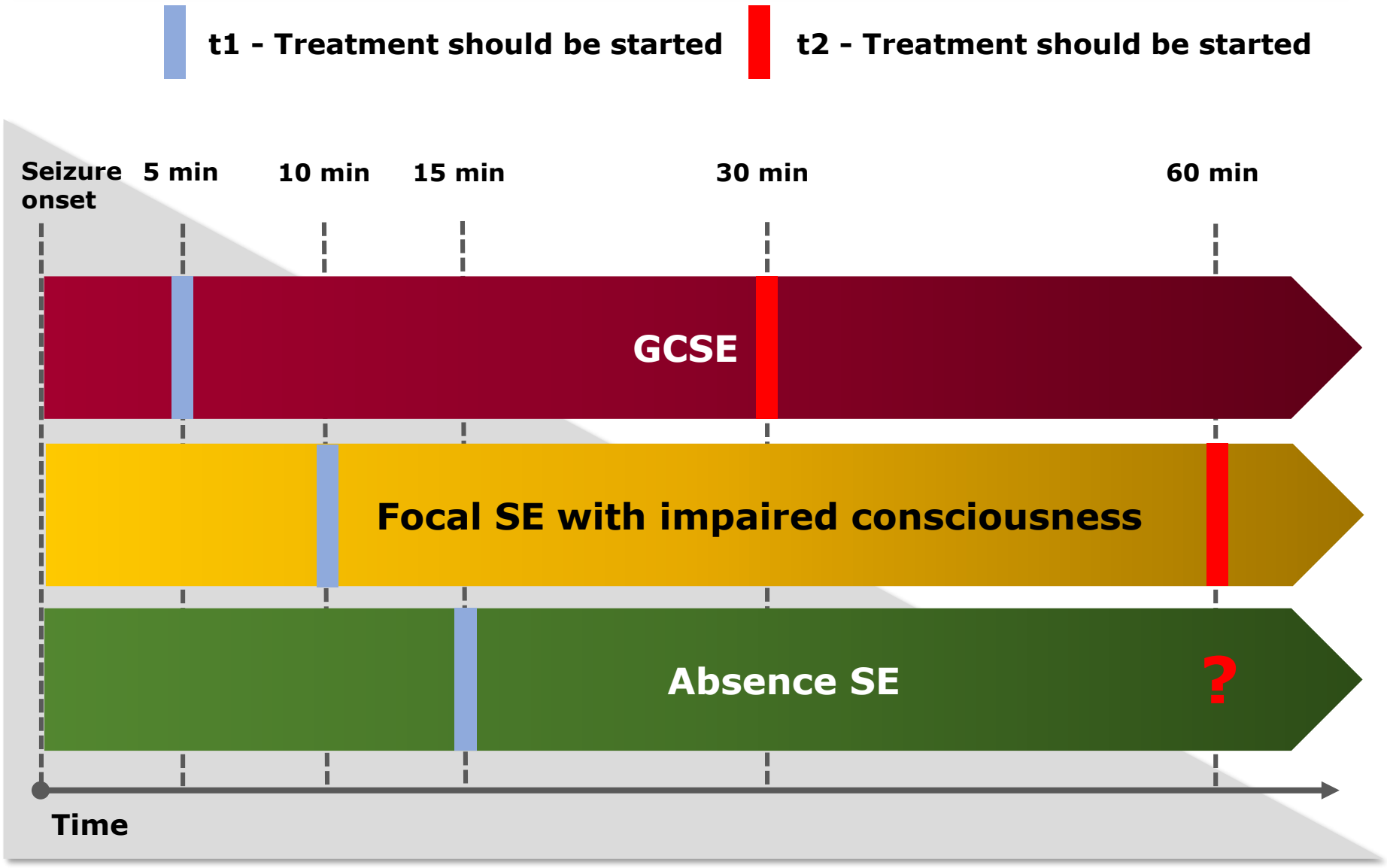
New definitions and classification system of SE

Status epilepticus is a prolonged seizure (**t1**) that might lead to long term consequences (**t2**) including neuronal death, neuronal injury, and alteration of neuronal networks, depending on type and duration of SE

Operational dimensions: → length of seizure (t1); → time (t2) to long term consequences

Trinka E et al, ILAE – Epilepsia 2015

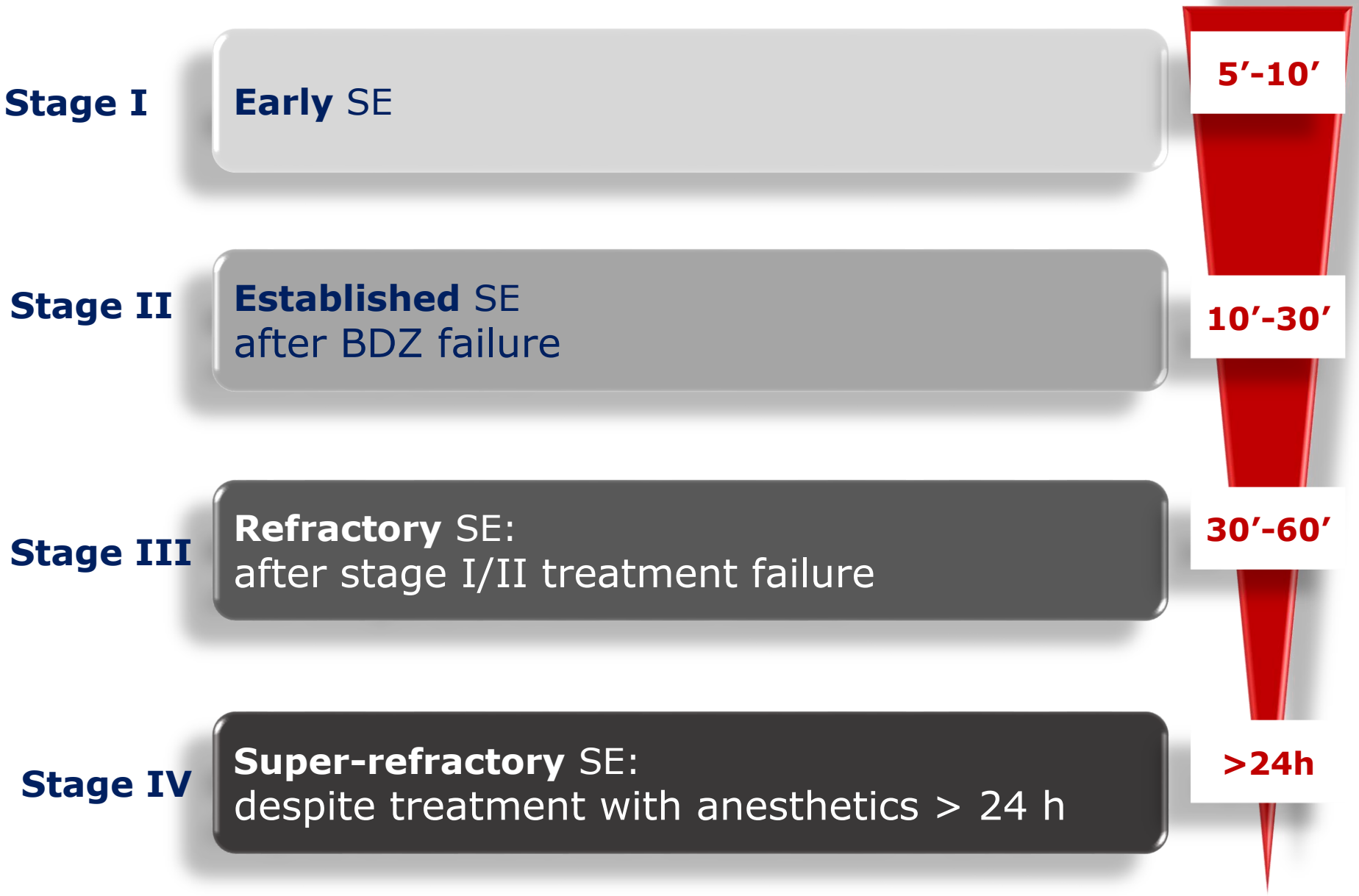
Acceptable time of initial treatment for various SE types recommended by the ILAE task force



Modified from Lee SK. Journal of Epilepsy Research 2020

Basic principles of treatment

SE stages according to time and treatment response



Trinka & Kalviainen, Seizure 2017

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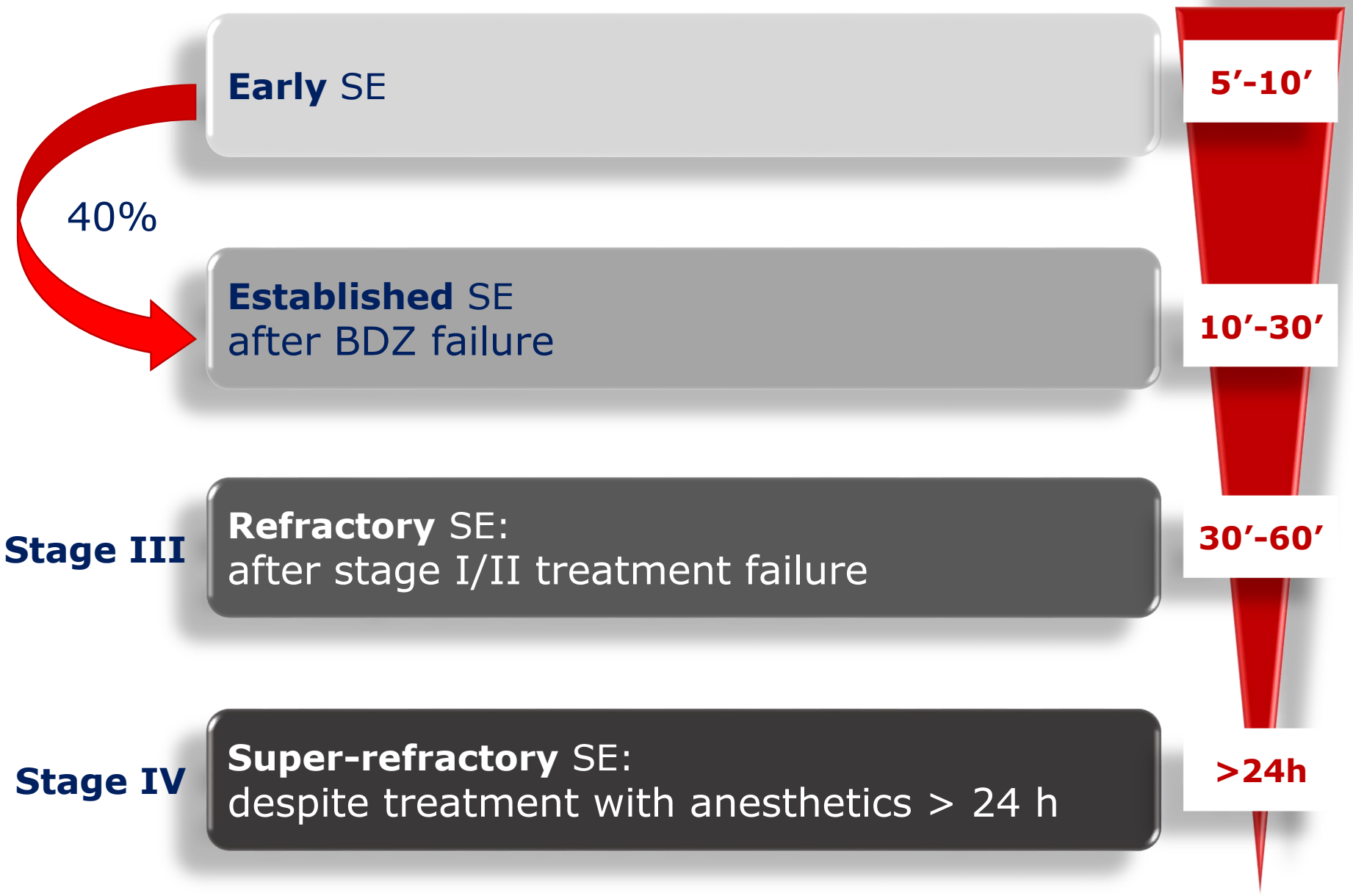

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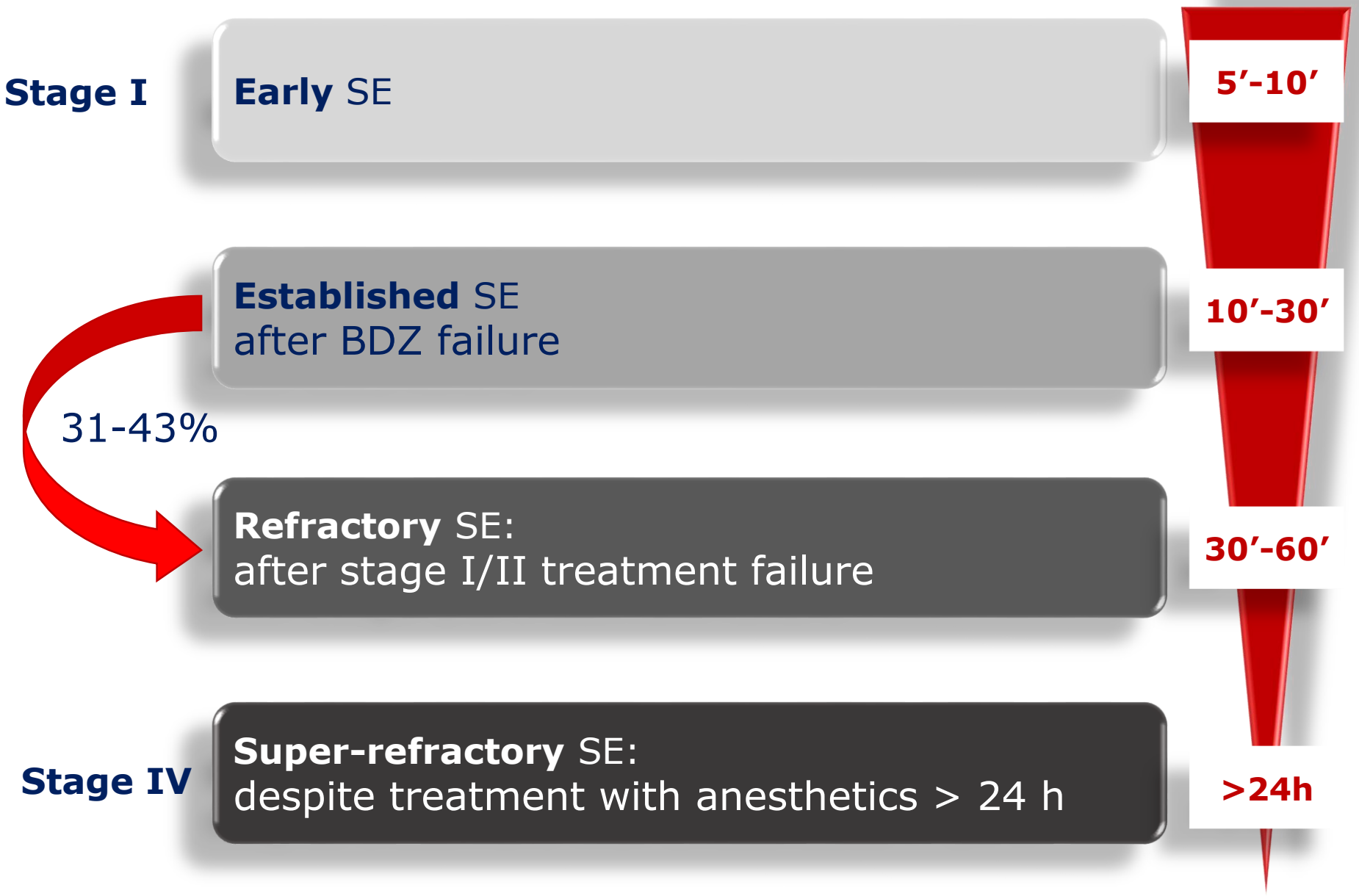


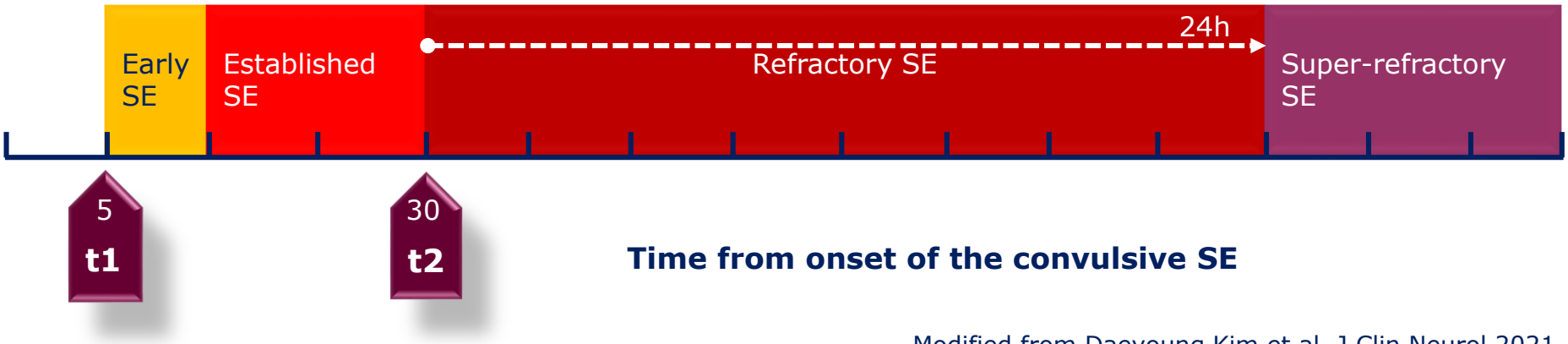
Trinka & Kalviainen, Seizure 2017

Treatment options for SE at different stages

- IV LZP 0.1 mg/kg (up to 4 mg; max 2 mg/min; may repeat once)
- IV DZP 0.15–0.2 mg/kg (up to 10 mg; max 5 mg/min; may repeat once)
- IM/IV MDZ 0.2 mg/kg (up to 10 mg)

- IV PHT 15–20 mg/kg (max 50 mg/min)
- IV FPHT 15–20 mg PE/kg (max 150 mg PE/min)
- IV PB 10–30 mg/kg (max 100 mg/min)
- IV VPA 15–45 mg/kg (max 10 mg/kg min)
- IV LEV 60 mg/kg (up to 4,500 mg; max 6 mg/kg/min)
- IV LCM 200–600 mg

- IV MDZ 0.2 mg/kg bolus, followed by CI at 0.05–2 mg/kg/h, titrated to achieve an EEG seizure cessation
- IV PPF 1–2 mg/kg bolus, may repeat up to 5 mg/kg, followed by CI at 5–10 mg/kg/h, down-titrated to maintain a BS
- IV THP 1–5 mg/kg bolus, followed by CI at 0.5–5 mg/kg/h, titrated to achieve a BS
- IV PTB 5–15 mg/kg bolus, followed by CI at 0.5–5 mg/kg/h, titrated to achieve a BS
- IV KET 0.5–4.5 mg/kg bolus, followed by CI at 0.3–5 mg/kg/h, titrated to achieve an EEG seizure cessation



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Role of old ASMs

The Newer, the Better?

Results of the studies with bromide in the early 1900 (Turner WA)

showing the general results of prolonged bromide medication in 366 cases treated at the Queen Square Hospital.

Cases of arrest	-	86 or 23·5 per cent.	
Cases showing improvement	-	105 or 28·7	„
Confirmed cases	-	175 or 47·8	„
TOTALS	-	366 100	„

52.2%

These figures are in general harmony with the observations of some other writers on the subject, notably Binswanger,[1] who refers to the result of bromide treatment in the Stephansfeld Institute for Epileptics in the following table, although the total number of cases on which the observations were made is not stated:

Arrest of seizures during treatment	-	23·3 per cent.
Diminution in frequency to one-half	-	40·0 „
No material change	-	36·6 „

63.3%

From D.E.Scott, "La storia della terapia dell'epilessia", Memento Medico, 1993

ASMs comparison in the treatment of CSE

Study	AEDs	Results (efficacy)
US Department of VA cooperative study:[33] RCT	IV lorazepam 0.1 mg/kg vs. IV phenytoin	Lorazepam > phenytoin
Leppik et al.[34] (double blind study)	IV diazepam 10 mg vs. IV lorazepam 4 mg	Equal efficacy (diazepam 76% vs. lorazepam 89%)
RAMPART[35]	10 mg midazolam vs. 4 mg lorazepam	Midazolam > lorazepam (probably rate dependent)
Yasiry and Shorvon[36] (meta-analysis)	IV valproate, IV phenobarbital, IV levetiracetam, IV phenytoin (BZD refractory CSE)	VPA (75.7%), phenobarbital (73.6%), levetiracetam (68.5%) > phenytoin (50%)
ESETT (ongoing):[37] prospective RCT	Phenyoint, vlaporate, levetiracetam (BZD refractory CSE)	
Nakamura et al.[38]	Recurred seizure after control of SE by BZD: levetiracetam vs. fosphenytoin	Equal efficacy

AED, antiepileptic drugs; CSE, convulsive status epilepticus; RCT, randomized controlled trial; IV, intravenous; BZD, benzodiazepine; VPA, valproic acid; SE, status epilepticus.

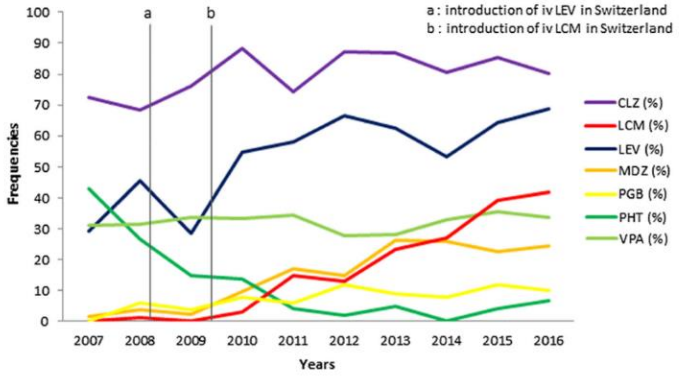
Lee SK. Journal of Epilepsy Research 2020

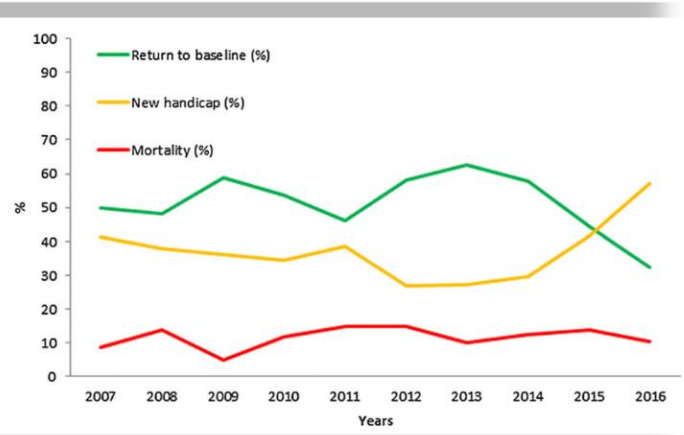
CNS Drugs (2017) 31:327–334
DOI 10.1007/s40263-017-0424-1

ORIGINAL RESEARCH ARTICLE

Newer Antiepileptic Drugs in Status Epilepticus: Prescription Trends and Outcomes in Comparison with Traditional Agents

Isabelle Beuchat[1] · Jan Novy[1] · Andrea O. Rossetti[1]





Key Points

The prescription of newer antiepileptic drugs (AEDs) in status epilepticus (SE) has markedly increased during the last decade, mostly due to the introduction of levetiracetam and lacosamide.

While mortality at hospital discharge did not significantly change, the use of newer AEDs was independently associated with higher SE refractoriness and disability at discharge.

These findings are potentially concerning and, awaiting comparative studies, may justify some caution in the routine use of newer AEDs in SE.

CNS Drugs (2018) 32:259–267
https://doi.org/10.1007/s40263-018-0509-5

REVIEW ARTICLE

Newer Antiepileptic Drugs for Status Epilepticus in Adults: What's the Evidence?

Isabelle Beuchat[1] · Jan Novy[1] · Andrea O. Rossetti[1]

Table 2 Advantages and disadvantages of newer versus traditional antiepileptic drugs

Variable	Newer AEDs	Traditional AEDs
Drug–drug interactions	Limited	Significant
Enzymatic induction/inhibition	Limited	Significant
Side effects	Minor	Potentially severe
Sedation	Minor	Potentially present
Teratogenicity	Some relatively "safe" (LEV), but several agents with no data	Well established, potentially severe (VPA)
Efficacy in status epilepticus	Not well-established	Well-established
Well-established protocol/dose/perfusion rate	No for most agents	Yes
Cost	High	Low
Worldwide availability	No	Yes
Impact on mortality	No clear evidence	No
Impact on disability	Possible association with greater disability	No
Rapid intravenous titration	Yes	Yes

AEDs antiepileptic drugs, *LEV* levetiracetam, *VPA* valproate

Key Points

Newer antiepileptic drugs show good tolerability, but no significant beneficial impact on outcome has yet been demonstrated in SE.

Good-quality randomized trials are urgently needed to determine the place of newer AEDs in SE.

Seizure: European Journal of Epilepsy 74 (2020) 20–25

Contents lists available at ScienceDirect

Seizure: European Journal of Epilepsy

journal homepage: www.elsevier.com/locate/seizure

Influence of new versus traditional antiepileptic drugs on course and outcome of status epilepticus

Caroline Reindl*, Maximilian I. Sprügel, Jochen A. Sembill, Tamara M. Mueller, Manuel Hagen, Stefan T. Gerner, Joji B. Kuramatsu, Hajo M. Hamer, Hagen B. Huttner, Dominik Madžar

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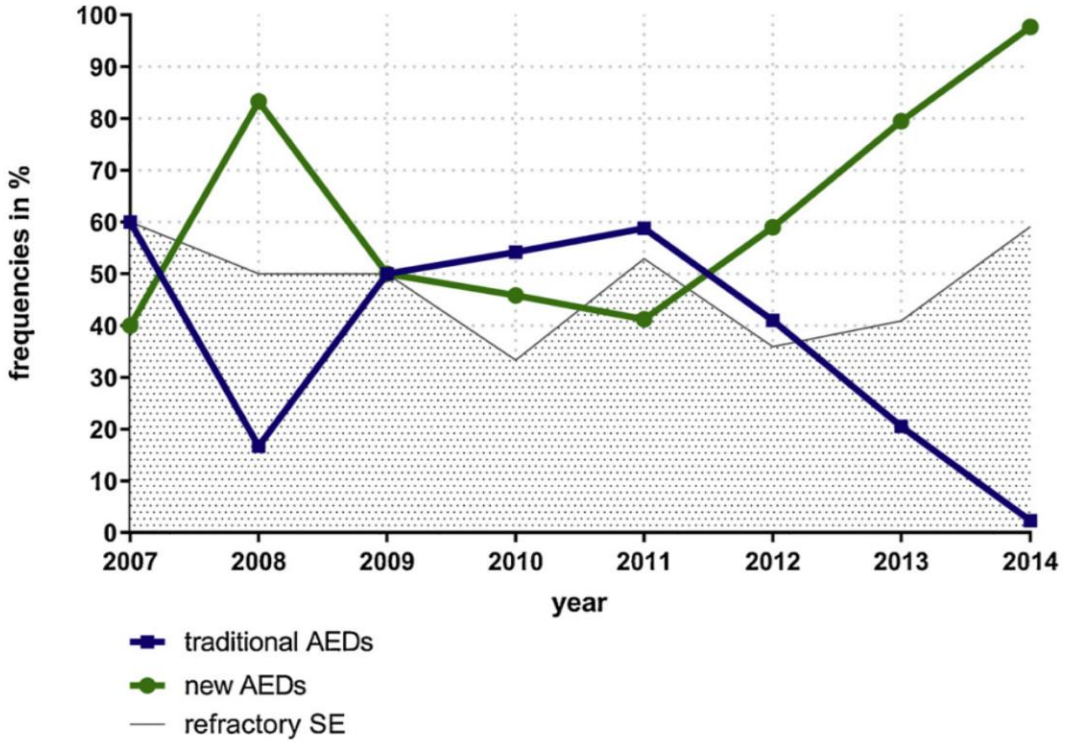
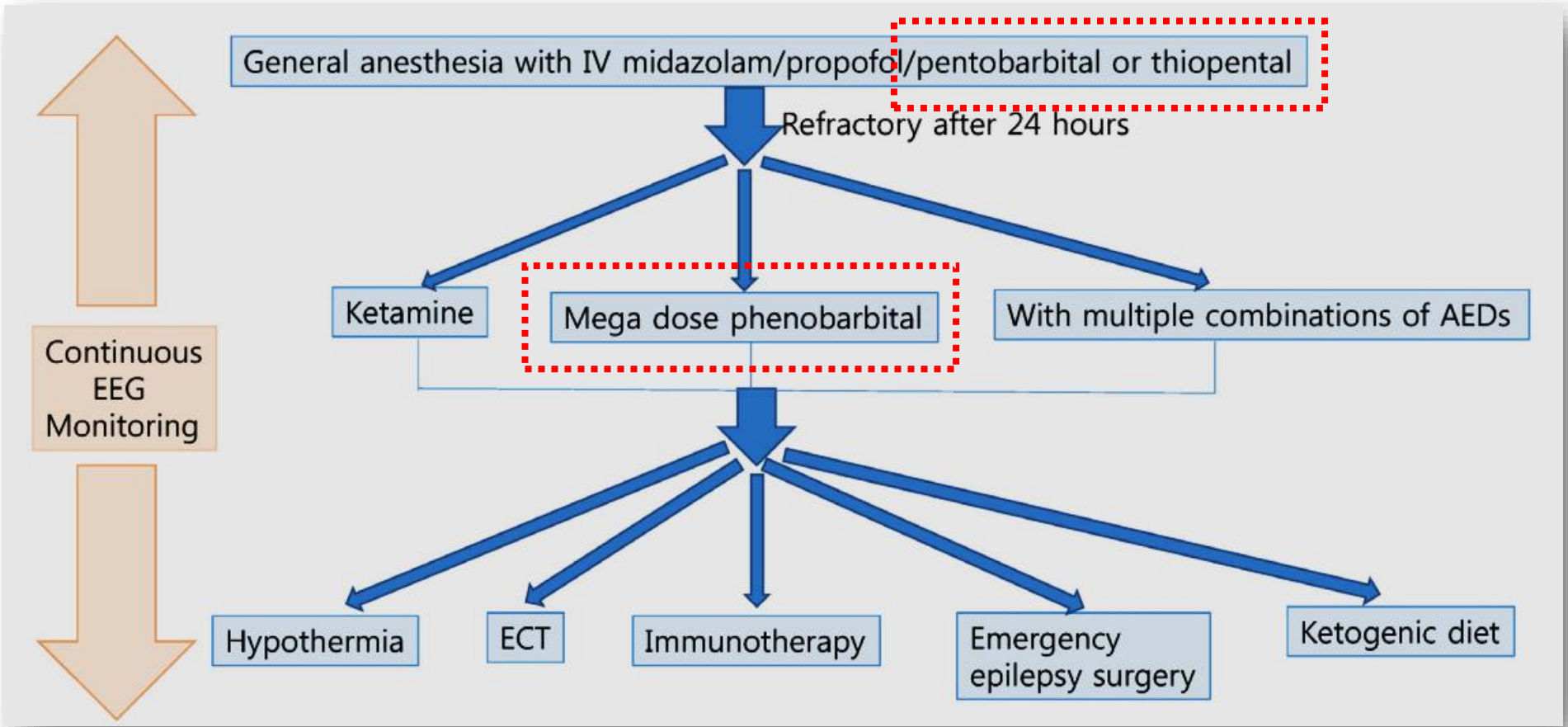


When the going gets tough: let's go to the back

Treatment algorithm for RSE and super-refractory SE



Lee SK. Journal of Epilepsy Research 2020

Status Epilepticus Severity Score (STESS)

	Features	STESS
Consciousness	Alert or somnolent/confused	0
	Stuporous or comatose	1
Worst seizure type	Simple-partial, complex-partial, absence, myoclonic*	0
	Generalized-convulsive	1
	Nonconvulsive status epilepticus in coma	2
Age	< 65 years	0
	≥ 65 years	2
History of previous seizures	Yes	0
	No or unknown	1
Total		0–6

* complicating idiopathic generalized epilepsy

Favorable score = 0–2