TABLE e-1

Probability of stopping seizures (SS) by different rescue medications. If the population was mixed we only analyzed the patients with convulsive SE that received only benzodiazepines before the second-line non-BZD AED.

Author and year (N = Number of SE episodes)	Setting and timeline	Type of study and level of evidence	Age of the patients (in years)	Dose	Definition of SE	Definition of seizures/SE stop	Probability of stopping prolonged seizures/SE	Additional details
PHENYTOIN								
Brevoord et al, 2005 [1] (N = 64)	Rotterdam, The Netherlands 1995-2001	Retrospective study	Median (range): 2 (0.04-16.45)	20 mg/Kg	Single seizure lasting more than 30 min or multiple seizures relapsing within 30 min without recovery of consciousness between each seizure. Patients refractory to benzodiazepine (iv or rectal midazolam sometimes preceded by rectal diazepam)	No clinical evidence of seizures during at least 30 min	19/64 (0.2969)	76% of patients were younger than 5yo
Agarwal et al, 2007 [2] (N = 50)	Kanpur, India 2004-2006	Randomized prospective study	Mean ± SD 27 ± 15.1	20mg/Kg	Continuous or repeated seizure activity for more than 5 minutes without recovery of consciousness. Patients refractory to IV diazepam	All motor or EEG seizure activity ceased ≤20 min from beginning of infusion and no return of seizure activity for 12h	42/50 (0.84) Among patients <18yo: 12/16 (0.75)	48% of patients had SE for >2h on presentation 16 episodes in patients younger than 18yo
Tiamkao & Sawanyawisuth, 2009 [3] (N = 37)	Khon Kaen, Thailand 2005-2007	Retrospective analysis	Adults ≥15yo	15-20 mg/Kg	≥2 generalized convulsions without full recovery of consciousness between	Seizure control that ceased within 30 minutes after the medication	17/37 (0.4595)	

					seizures or continuous convulsive activity for more than 10 min Refractory to iv diazepam	with no additional antiepileptic medication required for at least 24 hours after seizure cessation		
Alvarez et al, 2011 [4] (N = 70)	Lausanne, Switzerland 2006-2010	Retrospective analysis of a prospective registry	Mean ± SD 57.8 ± 18.1	20 mg/Kg	Continuous occurrence of seizures for >5 min or repeated epileptic seizures without intercurrent baseline recovery Patients refractory to IV benzodiazepine (clonazepam or lorazepam)	No need for another AED medication to control SE	41/70 (0.5857)	Excluded patients with postanoxic SE and patients <16yo
Ismail et al, 2012 [5] (N = 34)	Montreal, Canada 2002-2007	Retrospective study	Mean ± SD 1.8 ± 0.4 in episode with response to PHT 1.9 ± 0.3 in episodes with no response to PHT	15 mg/Kg	Febrile seizure lasting more than 15 min or ≥2 febrile seizures without return to normal state of consciousness between the episodes. Refractory to benzodiazepines (diazepam, lorazepam, or midazolam)	Ending clinical seizures before the end of the perfusion	9/34 (0.2647)	Only febrile SE
Tiamkao et al, 2013 [6] (N = 37)	Khon Kaen, Thailand 2003-2010	Retrospective study	Median (range) = 40 (16-85)	Mean ± SD 743 (116) mg	>5 min seizures or repeated seizures with no regain of consciousness between seizures Refractory	No clinical evidence of seizures	8/37 (0.2162)	

					to iv DZP 10mg			
Chitsaz et al, 2013 [7] (N = 15)	Isfahan, Iran 2009-2010	Randomized prospective study	Mean (SD) = 45.5 ± 20.4	20 mg/Kg	>5 min seizures or repeated seizures with no regain of consciousness between seizures Refractory to 2 doses of iv DZP 0.15 mg/Kg	Response to treatment within 12 hours	9/15 (0.6)	
Chakravarhi et al, 2015 [8] (N = 22)	Chandigarh, India 2012-2013	Prospective randomized open label study	Mean (SD) = 31.8 ± 12.7	20 mg/Kg	Continuous generalized convulsive seizure > 5 min or ≥ 2 seizures during which the patient does not regain normal sensorium Refractory to iv LZP	Clinical termination of seizure activity within 30 min of AED initiation	15/22 (0.6818)	21 generalized convulsive SE, 1 focal convulsive SE
Mundlarmuri et al, 2015[9] (N = 50)	Bangalore, India 2010-2013	Prospective randomized study	Mean (SD) = 33.2 ± 13.4	20 mg/Kg	Continuous generalized seizures ≥ 10 min or ≥ 2 seizures without complete recovery of consciousness in between Refractory to iv LZP 4-6mg	No recurrence of seizures after 30 min of completion of AED infusion with substantial improvement in sensorium over next 24 hours or sensorium did not improve substantially, but EEG excluded non-convulsive SE	34/50 (0.68)	
Gujjar et al, 2017 [10] (N = 30)	Muscat, Oman Time period not specified	Prospective study, open label	Mean ± SD 37 ± 19	20 m/Kg	Generalized tonic-clonic seizures > 5 min or recurrent generalized tonic-clonic	Cessation of clinical seizures, improvement in mental status, and	21/30 (0.7)	

					seizures with no regaining of consciousness between attacks or partial seizures > 10 min Refractory to initial benzodiazepine (LZP 4mg or DZP 5-10mg)	no recurrence of seizures over 24h		
PHENOBARBITAL								
Malamiri et al, 2012 [11] (N = 30)	Theran, Iran 2008-2010	Prospective randomized study	Median (range) 4 (3-11)	20 mg/Kg	Continuous generalized convulsive seizure lasting longer than 5 min No response to iv diazepam within 5 min	Termination of all convulsive activity within 20 minutes of initiation without respiratory depression or hypotension and without another convulsion within 1h	23/30 (0.7667)	Pediatric patients ≥2yo
Su et al, 2016 [12] (N = 37)	Beijing, China 2011-2015	Prospective randomized study	Mean (SD) = 37.1 ± 15	20 mg/Kg	≥5 min of continuous clinical and/or electrographic seizure activity without recovery between seizures. Refractory to 2 doses of DZP 0.2 mg/Kg	Cessation of clinical and EEG seizure activity within 20 min of AED administration	30/37 (0.8108)	All cases were generalized convulsive SE
Lee et al, 2016 [13] (N = 10)	Seoul, South Korea 2008-2013	Retrospective study	Median (range) 1.2 (0.08-13.9) in the 50 patients with SE or acute repetitive seizures	Median (range): 20mg/Kg (10-20) mg/Kg	≥5 min of continuous seizure activity or recurrent seizures without recovery of consciousness within 30 min Refractory to benzodiazep	Clinical seizure cessation within 30 minutes of completion of the infusion without recurrence during the following 24 hours	10/10 (1)	Excluded 40 patients with acute repetitive seizures with return to consciousness between episodes

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VALPROATE								
Agarwal et al, 2007 [2] (N = 50)	Emergency room and ICU in Kanpur, India from 2004 to 2006	Randomized prospective study	Mean (SD) = 27.4 ± 16.8	20mg/Kg	Continuous or repeated seizure activity for more than 5 minutes without recovery of consciousness. Patients refractory to IV diazepam	All motor or EEG seizure activity ceased ≤20 min from beginning of infusion and no return of seizure activity for 12h	44/50 (0.88) Among patients <18yo: 20/22 (0.9091)	40% of patients had SE for >2h on presentation 22 episodes in patients younger than 18yo
Olsen et al, 2007 [14] (N = 37)	Oslo, Norway After 2003	Prospective registry	Median (range): 45 (20-89)	25 mg/Kg	Ongoing epileptic activity for a minimum of 5 min or repeated epileptic seizures Refractory to diazepam	Seizure control at the end of the bolus dose	27/37 (0.7297)	Excluded 4 patients who received a bolus of iv propofol or iv barbiturate before valproate
Yu et al, 2007 [15] (N = 15)	Los Angeles, California Time period not specified	Retrospective study	Mean (range) 7.5 (0.08-19) [among the 40 patients in the study]	25 mg/Kg	Status epilepticus not further specified Refractory to lorazepam	Seizures stopped within 20 minutes of end of infusion	15/15 (1)	Excluded 22 patients with breakthrough seizures secondary to subtherapeutic VPA levels and 3 patients with SE who received PHT, PB, or both before VPA
Tiamkao & Sawanyawisuth, 2009 [3] (N = 12)	Khon Kaen, Thailand 2005-2007	Retrospective study	Adults ≥15yo	15-25 mg/Kg	≥2 generalized convulsions without full recovery of consciousness between seizures or continuous convulsive activity for more than 10 min Refractory to iv diazepam	Seizure control that ceased within 30 minutes after the medication with no additional antiepileptic medication required for at least 24 hours after seizure cessation	9/12 (0.75)	
Alvarez et	Lausanne	Retrospec	Mean ± SD	20 mg/Kg	Continuous	No need	44/59	Excluded

al, 2011 [4] (N = 59)	, Switzerland 2006-2010	tive analysis of a prospective registry	64 ± 18.9		occurrence of seizures for >5 min or repeated epileptic seizures without intercurrent baseline recovery Patients refractory to IV benzodiazepine (clonazepam or lorazepam)	for another AED medication to control SE	(0.7458)	patients with postanoxic SE and patients <16yo
Chen et al, 2011 [16] (N = 30)	Beijing, China 2007-2010	Prospective open-label randomized study	Mean ± SD 40.8 ± 23.2	30 mg/Kg	≥5 min of continuous seizures or ≥2 seizures between which there is incomplete recovery of consciousness Refractory to 2 doses of DZP iv 0.2mg/Kg	Control of clinical and EEG seizures within one hour of mediacation and no recurrence in 6 hours	15/30 (0.5)	Viral encephalitis as cause of SE in 40% of patients
Malamiri et al, 2012 [11] (N = 30)	Theran, Iran 2008-2010	Prospective randomized study	Median (range) 5 (3-16)	20 mg/Kg	Continuous generalized convulsive seizure lasting longer than 5 min No response to iv diazepam within 5 min	Termination of all convulsive activity within 20 minutes of initiation without respiratory depression or hypotension and without another convulsion within 1h	27/30 (0.9)	Pediatric patients ≥2yo
Tiamkao et al, 2013 [6] (N = 17)	Khon Kaen, Thailand 2003-2010	Retrospective study	Median (range) = 42 (16-76)	Mean ± SD 1000 (239) mg	>5 min seizures or repeated seizures with no regain of consciousness between seizures Refractory to iv DZP 10mg	No clinical evidence of seizures	8/17 (0.4706)	

Chitsaz et al, 2013 [7] (N = 15)	Isfahan, Iran 2009-2010	Randomized prospective study	Mean (SD) = 47.4 ± 14	20 mg/Kg	>5 min seizures or repeated seizures with no regain of consciousness between seizures Refractory to 2 doses of iv DZP 0.15 mg/Kg	Response to treatment within 12 hours	11/15 (0.7333)	
Mundlarmuri et al, 2015[9] (N = 50)	Bangalore, India 2010-2013	Prospective randomized study	Mean (SD) = 33.1 ± 12	30 mg/Kg	Continuous generalized seizures ≥ 10 min or ≥ 2 seizures without complete recovery of consciousness in between Refractory to iv LZP 4-6mg	No recurrence of seizures after 30 min of completion of AED infusion with substantial improvement in sensorium over next 24 hours or sensorium did not improve substantially, but EEG excluded non-convulsive SE	34/50 (0.68)	
Su et al, 2016 [12] (N = 36)	Beijing, China 2011-2015	Prospective randomized study	Mean (SD) = 45.3 ± 18.1	30 mg/Kg	≥5 min of continuous clinical and/or electrographic seizure activity without recovery between seizures. Refractory to 2 doses of DZP 0.2 mg/Kg	Cessation of clinical and EEG seizure activity within 20 min of AED administration	16/36 (0.4444)	All cases were generalized convulsive SE
Misra et al, 2017 [17] (N = 33)	Lucknow, India 2013-2016	Prospective randomized open-label study	Median (range): 40 (18-85)	30 mg/Kg	≥5 min of continuous convulsions or ≥ 2 convulsive seizures without full recovery.	Seizure cessation for 1 hour after the infusion of the study drug	23/33 (0.6970)	Exclusion of non-convulsive SE

					Refractory to 2 doses of IV LZP 4mg			
LEVETIRACETAM								
Knake et al, 2008 [18] (N = 13)	Marburg, Germany 2006-2007	Retrospective study	Median (range) 67 (35-90)	Mean ± SD loading dose: 846 ± 415 mg Mean ± SD maintenance dose over 24h: 2154 ± 1505 mg	≥30 min of continuous seizure activity or a series of seizures without return to full consciousness between seizures ≥30 min	No need for other AEDs	11/13 (0.8462)	Focal SE Patients did not receive PHT because of liver failure, elevated liver enzimes, cardiac arrhythmia, or comedication
Berning et al, 2009 [19] (N = 28)	Northern Germany (Osnabrück, Rotenburg, and Kiel) 2007-2008	Retrospective study	Median (p_{25}-p_{75}): 78 (68.3-84.5) low initial benzodiazepine Median (p_{25}-p_{75}): 68 (53-76.3) medium-high initial benzodiazepine	1000mg-3000mg	Convulsive seizures lasting at least 5 min or recurrent seizures without regaining full consciousness or partial seizures lasting at least 20 min. Low initial benzodiazepine: Not more than 2mg of LZP or a comparable dose of benzodiazepine. Medium-high initial benzodiazepine: Appropriate initial dose of benzodiazepine	Cessation of SE as shown by neurologic examination, EEG, or both. SE controlled within 30 minutes of LEV initiation	10/28 (0.3571) 3/8 (0.375) low initial benzodiazepine 7/20 (0.35) medium-high initial benzodiazepine	Semiology: 4 convulsive generalized, 6 subtle SE, 12 complex focal, 6 simple focal Semiology low initial benzodiazepine: 1 convulsive generalized, 1 subtle SE, 6 complex focal Semiology medium-high initial benzodiazepine: 3 convulsive generalized, 5 subtle SE, 6 complex focal, 6 simple focal
Eue et al, 2009 [20] (N = 33)	Bernburg, Germany 2006-2008	Prospective study	Mean (range) 67 (43-92) for the whole population of 43 patients with convulsive	1000mg	Generalized convulsive SE ≥ 5min or simple, complex focal, myoclonic, and SE ≥ 30 min.	Cessation of clinical seizures within 3 min of LEV administration	16/33 (0.4849) 0/8 (0) in generalized tonic-clonic SE 11/18 (0.6111) in	Semiology: 8 generalized tonic-clonic, 18 convulsive complex focal, 5 simple

			and non-convulsive SE		No response to benzodiazepines (lorazepam 2-6mg or diazepam 5-10mg)		complex partial 3/5 (0.6) in simple focal 2/2 (1) in myoclonic SE	focal, 2 myoclonic Excluded patients with nonconvulsive SE and subtle SE
Gámez-Leyva et al, 2009 (N = 16)	Salamanca and Santander, Spain 2007-2008	Retrospective study	Median (p25-p75): 77 (64.8-84.8)	1000 mg in the full cohort of 34 patients	≥30 min of continuous seizures or a series of seizures without return to full consciousness for at least 30 min and/or confirmation of SE on EEG Refractory to 20mg of iv DZP	No seizures within, at most, 8h after iv LEV, no other AED needed, and no recurrence of SE during the hospital stay	10/16 (0.625)	7 partial secondarily generalized SE, 5 partial motor SE, 3 complex partial SE, 1 primary generalized SE. Excluded patients who received iv PHT or iv VPA before LEV. Considered a threshold for response of 8h since iv LEV
Alvarez et al, 2011 [4] (N = 58)	Lausanne, Switzerland 2006-2010	Retrospective analysis of a prospective registry	Mean ± SD 66.1 ± 14.9	20 mg/Kg	Continuous occurrence of seizures for >5 min or repeated epileptic seizures without intercurrent baseline recovery Patients refractory to IV benzodiazepine (clonazepam or lorazepam)	No need for another AED medication to control SE	30/58 (0.5172)	Excluded patients with postanoxic SE and patients <16yo
Standish et al, 2011 [21] (N = 9)	Wilmington, DE 2007-2008	Retrospective study	Median (p25-p75): 4 (2-8)	Median (range): 33.3 (16-98.8) mg/Kg in the 20 patients where LEV was used not as second-line after initial benzodiaze	Clinical diagnosis of SE. Refractory to initial benzodiazepine (LZP, MDZ, or DZP)	No need for another AED to control SE	9/9 (1)	Excluded patients where LEV was used as first line without prior benzodiazepine or after use of other non-benzodiazepine AED

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Atmaca et al, 2015 [22] (N = 10)	Istanbul, Turkey 2010-2013	Prospective study	Median (p25-p75): 51 (45.8-52.8)	Median (p25-p75): 2000 (2000-3000) mg	Convulsive SE ≥ 5 min Refractory to benzodiazepine	Cessation of clinical seizures	7/10 (0.7)	Excluded patients with non-convulsive SE and epilepsia partialis continua
Chakravarhi et al, 2015 [8] (N = 22)	Chandigarh, India 2012-2013	Prospective randomized open label study	Mean (SD) = 39 ± 18.4	20 mg/Kg	Continuous generalized convulsive seizure > 5 min or ≥ 2 seizures during which the patient does not regain normal sensorium Refractory to iv LZP	Clinical termination of seizure activity within 30 min of AED initiation	13/22 (0.5909)	20 generalized convulsive SE, 2 focal convulsive SE
Mundlarmuri et al, 2015[9] (N = 50)	PHT Bangalore, India 2010-2013	Prospective randomized study	Mean (SD) = 34.8 ± 13.6	25 mg/Kg	Continuous generalized seizures ≥ 10 min or ≥ 2 seizures without complete recovery of consciousness in between Refractory to iv LZP 4-6mg	No recurrence of seizures after 30 min of completion of AED infusion with substantial improvement in sensorium over next 24 hours or sensorium did not improve substantially, but EEG excluded non-convulsive SE	39/50 (0.78)	
Lee et al, 2016 [13] (N = 12)	Seoul, South Korea 2008-2013	Retrospective study	Median (range) 1.7 (0.17-14.4) in the 38 patients with SE or acute repetitive seizures	Median (range): 30mg/Kg (20-30) mg/Kg	≥5 min of continuous seizure activity or recurrent seizures without recovery of consciousness within 30 min Refractory to	Clinical seizure cessation within 30 minutes of completion of the infusion without recurrence during the following 24 hours	4/12 (0.3333)	Excluded 26 patients with acute repetitive seizures with return to consciousness between episodes

					benzodiazepines			
Gujjar et al, 2017 [10] (N = 22)	Muscat, Oman Time period not specified	Prospective study, open label	Mean ± SD 38 ± 19	30 mg/Kg	Generalized tonic-clonic seizures > 5 min or recurrent generalized tonic-clonic seizures with no regaining of consciousness between attacks or partial seizures > 10 min Refractory to initial benzodiazepine (LZP 4mg or DZP 5-10mg)	Cessation of clinical seizures, improvement in mental status, and no recurrence of seizures over 24h	18/22 (0.8182)	
LACOSAMIDE								
d'Orsi et al, 2016 [23] (N = 9)	Foggia and Rome, Italy 2011-2015	Prospective observational study	Mean (range): 60 (45-85)	200 mg	Convulsive SE that did not respond to benzodiazepines (IV DZP)	Cessation of SE within 20 min and without other AED administered	7/9 (0.7778)	
Misra et al, 2017 [17] (N = 33)	Lucknow, India 2013-2016	Prospective randomized open-label study	Median (range): 40 (18-90)	400 mg	≥5 min of continuous convulsions or ≥ 2 convulsive seizures without full recovery. Refractory to 2 doses of IV LZP 4mg	Seizure cessation for 1 hour after the infusion of the study drug	21/33 (0.6364)	

Legend: AEDs: Antiepileptic drugs. **DZP:** Diazepam. **EEG:** Electroencephalogram. **h:** Hours. **ICU:** Intensive care unit. **h:** hours. **IV:** Intravenous. **LAC:** Lacosamide. **LEV:** Levetiracetam. **LZP:** Lorazepam. **MDZ:** Midazolam. **min:** Minutes. **p_{25}-p_{75}:** 25^{th}-75^{th} quartile. **PB:** Phenobarbital. **PHT:** Phenytoin. **SD:** Standard deviation. **SE:** Status epilepticus. **VPA:** Valproate. **yo:** Year-old.

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