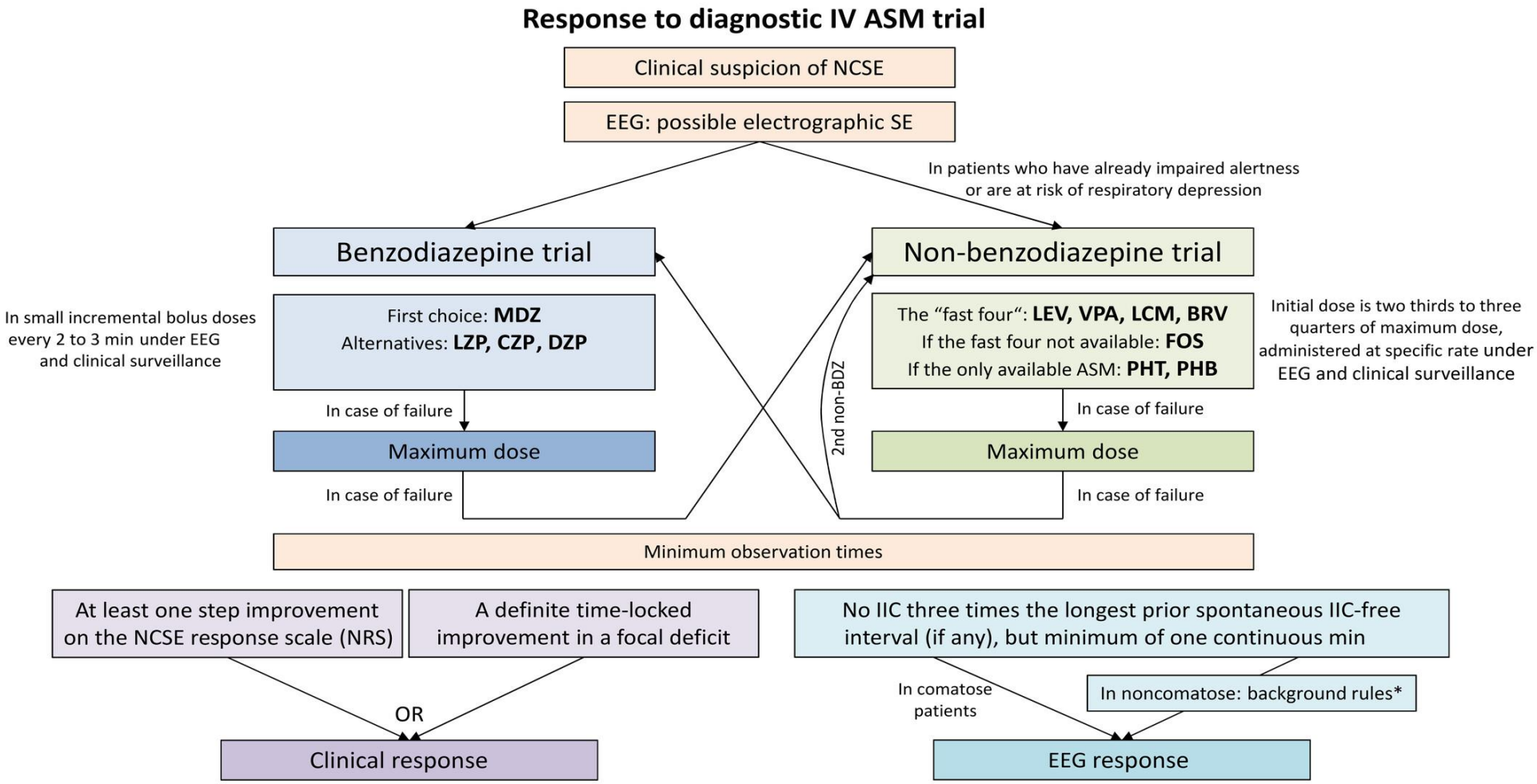
Antiseizure Medication Trial for Possible Status Epilepticus or Ictal-Interictal Continuum (IIC)



Overview of the diagnostic IV ASM trial recommendations.

Ictal-Interictal Continuum (IIC) Definition:

- Any PD or SW pattern that averages >1.0 Hz but ≤2.5 Hz over 10 s (>10 but ≤25 discharges in 10 s); OR
- Any PD or SW pattern that averages ≥0.5 Hz and ≤1 Hz over 10 s (≥5 and ≤10 discharges in 10 s), and has a plus modifier or fluctuation; OR
- Any lateralized RDA averaging >1 Hz for at least 10 s (at least 10 waves in 10 s) with a plus modifier or fluctuation;

AND

- Does not qualify as an ESz or ESE
  - Electrographic seizure (ESz)
    - Rhythmic or periodic pattern > 2.5 Hz for > 10 seconds
    - Evolving pattern > 10 seconds
  - Electrographic status epilepticus (ESE)
    - 10 minutes of continuous ESz
    - >20% of a 60 minute period

Antiseizure Medication Trial (identifying Nonconvulsive Status Epilepticus)

This is not a treatment for unequivocal seizures/status epilepticus but is instead a method to attempt to differentiate between seizure activity and interictal activity, when the EEG pattern shows periodic discharges or LRDA on the IIC with a gap between the EEG pattern and the paraclinical data (Both EEG and neuro exam looks worse than expected based on clinical situation).

- A positive response to an ASM is defined as 1) Resolution of concerning EEG pattern along with 2) Unequivocal clinical improvement. A positive response results in the IIC pattern being recategorized as clinical electrographic status epilepticus.
- Testing requires review of EEG and neuro exam before ASM is given and after ASM is given. This requires clinical and EEG supervision while medications are given.
- Clinical response = improvement in focal neurologic deficit time locked to EEG (aphasia, clonic activity, etc) or improvement in consciousness which can be measured using the Nonconvulsive Status Epilepticus Response Scale (NRS). This improvement should last > 1 minute.

Level 10: Normal
Level 9: Speaks or writes words with clear sense, oriented to person, year, and city or region, but behavior or performance different than normal
Level 8: Speaks or writes words with clear sense, but disoriented to person, year, and city or region
Level 7: Speaks or writes words or syllables, incomprehensible or confused
Level 6: Follows commands (verbally or by demonstration) (e.g., open/close eyes, raise arms, say "1, 2, 3")
Level 5: Directed gaze to examiner (or responsive vertical eye movement in locked-in syndrome), does not follow any commands (neither verbal nor by demonstration)
Level 4: Opens eyes spontaneously or to verbal stimulus or to light touch (no directed gaze), does not follow any commands
Level 3: Opens eyes to (strong) tactile stimulus (right or left shoulder, nose), does not follow commands (neither verbal nor by demonstration)
Level 2: Localizes to/wards off painful stimuli
Level 1: No purposeful response to painful stimuli

- Non-benzodiazepines should be used first in patients who already have impaired alertness or are at risk of respiratory depression.
- Non-benzodiazepine should be given at two thirds to three quarters of the maximum loading dose and if there is no improvement after 15 minutes, give the remainder of the loading dose.

Non-BZD	Levetiracetam	Valproate	Lacosamide	Fosphenytoin
Starting dose	40 mg/kg	30 mg/kg	6 mg/kg	15 mg PE/kg
Administration time	5 min	5 min	10 min	10-15 min (maximum 150 mg/min)
After minutes 15 if there is no improvement, give additional boluses up to maximum dose based on weight or absolute value (whichever is lower):				
Max (weight based/absolute)	60 mg/Kg or 4500 mg	40 mg/Kg or 3000 mg	8 mg/Kg or 600 mg	20 PE/Kg or 2000 PE

- An immediate positive response is more likely with a benzodiazepine, but results are often indeterminate as patient becomes sedated and no clinical improvement is noted, so use low doses and repeat dose every 2-5 minutes if no EEG improvement.

	Midazolam	Lorazepam	Clonazepam	Diazepam
Starting dose	**1 mg**	**.5 mg**	**.25 mg**	**4 mg**
If there is no EEG response, give incremental doses (same as starting doses) every 2–3 min (under EEG and clinical monitoring) up to a maximum dose of (whichever is lower):				
Maximum dose, weight based	.2 mg/kg	.1 mg/kg	.05 mg/kg	.25 mg/kg
Maximum dose, absolute	5 mg	2.5 mg	1.25 mg	20 mg

- A delayed response (> 2 hours) is more likely with loading a non-benzodiazepine ASM such as levetiracetam, fosphenytoin, valproate, or lacosamide.
- A positive EEG change includes an interval with no IIC pattern for over 3 times the longest prior spontaneous break in IIC or at least a 1 minute break if IIC activity is continuous

References:

Hirsch LJ, Fong MWK, Leitinger M, LaRoche SM, Beniczky S, Abend NS, et al. American clinical neurophysiology Society's standardized critical care EEG terminology: 2021 version. J Clin Neurophysiol. 2021; 38(1): 1–29. https://doi.org/10.1097/WNP.0000000000000806

Leitinger M, Gaspard N, Hirsch LJ, Beniczky S, Kaplan PW, Husari K, et al. Diagnosing nonconvulsive status epilepticus: defining electroencephalographic and clinical response to diagnostic intravenous antiseizure medication trials. Epilepsia. 2023; 64: 2351–2360. https://doi.org/10.1111/epi.17694

O'Rourke D, Chen PM, et al. Response Rates to Anticonvulsant Trials in Patients with Triphasic-Wave EEG Patterns of Uncertain Significance. Neurocrit Care. 2016 Apr;24(2):233-9.