ESETT ELIGIBILITY OVERVIEW

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Eligibility

• Age
• Convulsive Status
• Benzos
• Not excluded
Eligibility

• Age
  • 2 years to < 18 years (Pediatric)
  • 18 years to 65 years (Adult)
  • > 65 years (Geriatric)
Eligibility

- Convulsive status
  - Generalized tonic clonic
    - May have started focally, then generalized
    - May have been generalized but patient remains unconscious and exhibiting focal convulsions (i.e. motor activity)
  - Unresponsive to pain (no pseudoseizures please)
  - At least 5 minutes in total duration
Eligibility

• Benzos
  • Adequate dose
    • Diazepam
    • Lorazepam
    • Midazolam
  • Within last 5-30 minutes
    • At least 5 minutes ago
    • Not more than 30 minutes ago
  • Prehospital meds count (including home meds)

<table>
<thead>
<tr>
<th></th>
<th>Adult (≥40 kg)</th>
<th>Child (&lt; 40 kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diazepam</td>
<td>10 mg</td>
<td>0.3 mg/kg IV</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>4 mg</td>
<td>0.1 mg/kg</td>
</tr>
</tbody>
</table>
| Midazolam | 10 mg          | 0.3 mg/kg IM  
                  |                | 0.2 mg/kg IV    |
Eligibility Summary

• The 5:30 rule
  • At least 5 minutes of convulsive activity
  • Last benzos at least 5 minutes ago
  • Last benzos not more than 30 minutes ago
Eligibility

- Excluded
  - Known pregnancy
  - Prisoner
  - Patient opted out of study
  - Already treated with a second line agent
  - Already sedated/paralyzed/intubated
  - Acute traumatic brain injury
  - Post cardiac arrest/anoxic seizures
  - Known metabolic disorder
  - Known liver disease
  - Known severe renal disease
  - Hypoglycemia (<50) or hyperglycemia (> 400)
  - Known allergy to FOS, LEV, VPA

  - Ethics/regulatory considerations
  - Efficacy confounders
  - These diseases are different
  - Drug toxicity/metabolism
  - Treatment is glucose management
Let’s Review: Vignette # 1

A 2 y.o. male began seizing at home (generalized TC). Parents gave Diastat 10 mg rectally and EMS gave 2 mg of midazolam (Versed) IM. He has not woken yet and on ED arrival he has rhythmic twitching of the left hand and forearm. With regard to his eligibility,

A. He is not eligible because he is too young
B. He is not eligible because he did not receive enough benzodiazepines
C. He is not eligible because he is not in status
D. He is eligible for enrollment and should be randomized
E. He is not eligible because his seizures are focal only

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![Bar chart showing percentages: A. 0%, B. 35%, C. 4%, D. 55%, E. 6%]
Let’s Review: Vignette # 2

A 2 y.o. male began seizing at home earlier in the day. Parents gave Diastat 10 mg rectally and EMS gave 2 mg of midazolam (Versed) IM en route. He has been seizure-free in the ED for one hour. He starts to have generalized TC seizures. With regard to his eligibility,

A. He is not eligible until he seizes for at least 5 minutes
B. He is not eligible because he did not receive enough benzodiazepines
C. He is not eligible because his benzodiazepines were too long ago
D. A & C
E. B & C

![Bar chart showing the percentage of each option: A. 9%, B. 2%, C. 2%, D. 82%, E. 5%]
Let’s Review: Vignette # 3

A 2 y.o. male began seizing at home earlier in the day. Parents gave Diastat 10 mg rectally at 5 minutes. No additional meds given in ambulance. He arrives at the ED actively convulsing 40 minutes after seizure onset.

A. He is eligible because continues to have seizures despite diazepam and should be randomized.

B. He is not eligible because he only received rectal diazepam and needs to receive a dose of IV or IM benzodiazepenes before being eligible

C. He is not eligible because his benzodiazepines were too long ago

D. He is not eligible because he is too young

E. B & C
Let’s Review: Vignette # 4

A 6 year old male with Lennox-Gastaut arrives in the ED with repeated brief convulsions with no recovery in between. Child is currently on Valproate, leviteracetam and clobazam. He is well known to ED staff with multiple visits, often in setting of intercurrent illness. Parents gave 10 mg rectal diazepam gel at home and he received 7.5 mg of midazolam IM in route. He is witnessed to still have brief 30-45 sec convulsions in ED without recovery in between.

A. He is eligible because continues to have seizures despite diazepam and midazolam and should be randomized.
B. He is not eligible because he is on valproate and leviteracetam
C. He is not eligible because he is not in status
D. He is not eligible because Lennox-Gastaut is not a localization related epilepsy
E. B & C
Enrollment Overview

-00:30 to -00:05 cumulative dose of benzodiazepine must be ≥ adequate with last dose given > 5 and < 30 min prior to study treatment

Speculative timing of ictus (ICT), ED arrival (ED), and benzo doses (B)

If sz’s are continuing or recurring clinical team assesses eligibility. Kits are randomized ahead. Clinical team pulls “use next” kit (by age tier) and prepares infusion Study team is activated

00:00 enrollment/randomization

00:00 - 00:10 study drug infusion

00:00 - 01:00 observe without intervention

00:10 - 00:20 rescue if sz recurs or prn

00:20 - 01:00 rescue medication given if ongoing sz

01:00 primary outcome assessment

Established Status Epilepticus Treatment Trial
Enrollment

- Page the Study Team
- Use estimated weight if unknown (Broselow, etc)
- Open the "Use Next" Box for correct age group
- Start the Protocol Assist Device
- Use the Dosing Chart to draw up medication
- Second nurse confirm correct volume
- IV or IO route
- Use pump to deliver over 10 minutes
- Maintain usual care (monitoring, etc.)
### Dosing

<table>
<thead>
<tr>
<th>Subject Wt (kg)</th>
<th>Infusion Vol. (mL)</th>
<th>Infusion Rate (mL/min) over 10 min</th>
<th>FOS dose (mg)</th>
<th>LEV dose (mg)</th>
<th>VPA dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.5</td>
<td>9</td>
<td>0.9</td>
<td>150</td>
<td>450</td>
<td>300</td>
</tr>
<tr>
<td>10</td>
<td>12</td>
<td>1.2</td>
<td>200</td>
<td>600</td>
<td>400</td>
</tr>
<tr>
<td>12.5</td>
<td>15</td>
<td>1.5</td>
<td>250</td>
<td>750</td>
<td>500</td>
</tr>
<tr>
<td>15</td>
<td>18</td>
<td>1.8</td>
<td>300</td>
<td>900</td>
<td>600</td>
</tr>
<tr>
<td>Etc.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥75</td>
<td>90</td>
<td>9</td>
<td>1500</td>
<td>4500</td>
<td>3000</td>
</tr>
</tbody>
</table>
Enrollment and Dosing

Open study box
remove study drug

Estimate weight:
Use Broselow like tape if necessary

<table>
<thead>
<tr>
<th>Wt. (kg)</th>
<th>Vol.</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.5</td>
<td>9</td>
</tr>
<tr>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>12.5</td>
<td>15</td>
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<td>15</td>
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<tr>
<td>70</td>
<td>84</td>
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<tr>
<td>75</td>
<td>90</td>
</tr>
<tr>
<td>&gt;75</td>
<td>90</td>
</tr>
</tbody>
</table>

Connect to patient IV catheter

Dial appropriate volume in the infusion pump. Press start
Enrollment

- $T_0 =$ start of study drug infusion
- $T_{10}:$ medication should be finished
- $T_{20}:$ assess patient for ongoing status
  - Clinical status persists $\rightarrow$ treatment failure $\rightarrow$ treat with another agent, intubate, etc.
  - Clinical status stopped $\rightarrow$ assess responsiveness and wait for patient to recover
- $T_{60}:$ primary outcome determination
Continuous EEG

• If this is part of your hospital’s usual care
• Secondary study
Vignettes for enrollment?

- IV falls out/infiltrates at T5 minutes
- Assist device fails
- Patient still in status at 20 minutes and study team has not arrived yet
- Cannot reach study team at all
- Patient becomes apneic at 10 minutes
Questions