

ESETT PHARMACOKINETIC- PHARMACODYNAMIC (PK/PD) STUDY

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Outline

- **Study progress**
- **Overview**
- **Procedures**
- **Questions**

Study Progress

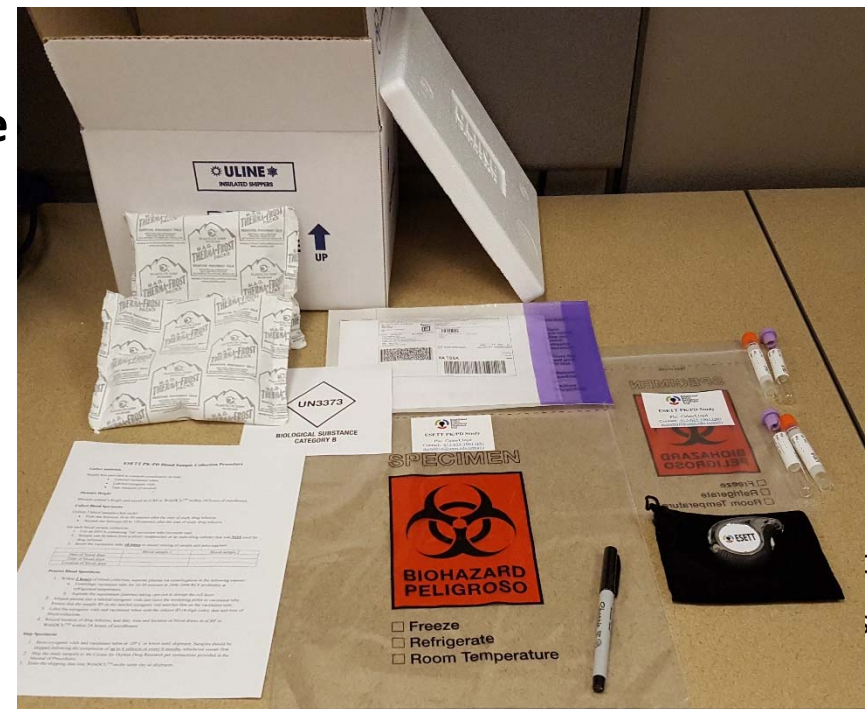
- **Contracts**
- **Training**
- **Site initiation**
- **Subject enrollment**

Importance of PK/PD Study

- **Determine whether drug concentrations help explain responses (seizure cessation/AEs).**
- **Aim: Relate drug exposure with seizure cessation and the key secondary outcomes.**
- **Outcomes:**
 - **Better understand the results from ESETT.**
 - **Provide guidance on how best to use FOS, LEV, and VPA for treatment of SE in children.**

Materials

- **Supply kits have been provided to research coordinators and include:**
 - Labeled 7-mL lavender top vacutainer tubes
 - Labeled 5 mL cryogenic vials
 - Sharpie®
 - Tape measure
 - Sample collection procedures quick guide
 - Case Report Form
 - Biohazard bags
 - Shipping materials (cold packs, insulated boxes, biological substance label, and pre-paid FEDEX shipping labels)

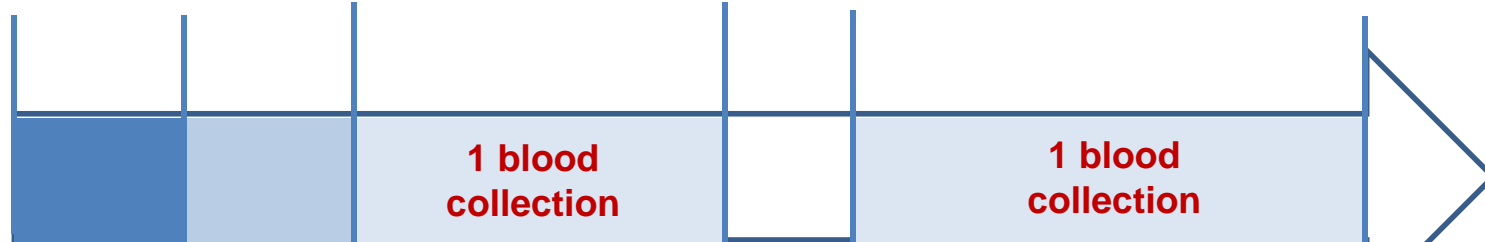


PK/PD Sample Collection Timetable

- **Collect two blood samples (2.5 mL/sample)**
 - **One sample between 20-50 min and a second sample between 60-120 min from the start of drug infusion**
 - Record exact blood collection time
 - If unable to collect sample within window, draw sample when possible because drug concentrations will still be used.

enrollment/
randomization

00:00 00:10 00:20 00:50 00:60 02:00



study
drug
infusion

observe



Measurement of Height

- **Measure the patient's height (using the official ESETT tape measure) and record in the medical record, other appropriate source document, or directly in the ESETT PK eCRF.**
- **If height can't be measured, a previously recorded height or estimated height should be recorded.**

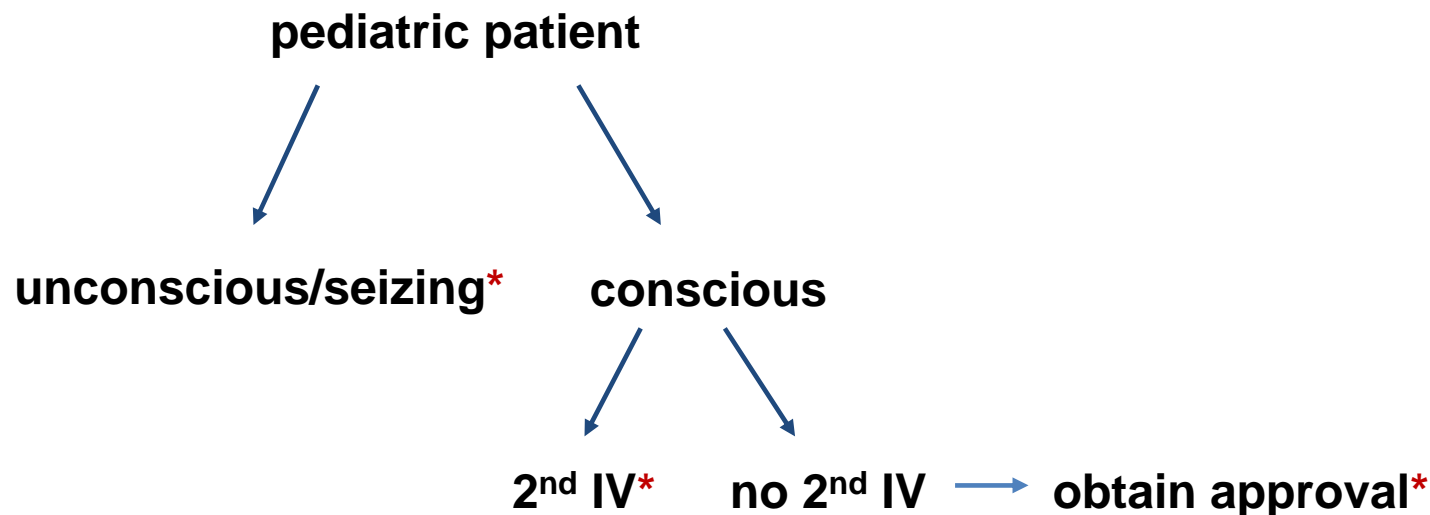


Consenting Considerations

- **Blood collection, as part of the ESETT protocol, will occur under exception from informed consent (EFIC).**
- **If patient, parent, or other legally authorized representative (LAR) withdraws consent to continue participation from ESETT, they have also withdrawn from the PK/PD study.**
- **PK/PD ancillary study should not affect ESETT**
 - **Even if patient, parent or other LAR informs the study team that he/she does not want blood sample(s) collected, he/she can still participate in ESETT.**

Consenting Considerations

- For children who are conscious and do not have a second IV catheter available for blood collection, the LAR should be asked if blood may be drawn by venipuncture for research purposes. If the answer is no, blood should not be collected.



* collect sample

Talking Points for Parents/LAR

- **The blood will be used to measure the amount of study drug in the blood.**
- **Measuring the amount of the drug in the blood may help us understand why seizures did or did not stop.**
- **We will be able to use this information to help us decide the best dose for future patients when they are given these same medications.**

Other Reminders

- **If the first blood sampling window is missed, please take 2 samples in the second window. If you can only obtain 1 sample, please collect it.**
- **Fill out ESETT PK/PD eCRF for every ESETT subject.**

Contacts

- ESETT PK/PD study team at esett-pkpd@umich.edu
- Lisa Coles at 612-624-1861 (office)
- James Cloyd at 612-624-4609 (office)

References

- Manual of Procedures
- 1 page quick guide

Thank you!

- **Special thanks to UC Davis and Nationwide Children's for sharing their experiences!**
- **Integrate blood sampling into the ESETT process.**

Frequently Asked Questions

- **Can a blood sample drawn from the drug infusion site be used?**
 - **Answer: No.** Studies have shown that even with multiple flushing steps, drug concentrations are very often artificially high in such samples. If blood is inadvertently drawn from the drug infusion site, please discard sample and record in the PK blood collection eCRF. While this is a procedural deviation, it is **NOT** a protocol deviation.
- **Can blood drawn from a site used to deliver fluids or other study medication be used?**
 - **Answer: Yes.** Blood can be drawn from any site **NOT** used for study drug infusion.
- **What should I do if we collect only one blood sample?**
 - **Answer: Process and ship the sample as specified.** While we expect to obtain 2 samples from most subjects, a single sample from a subset of patients will still be valuable. This is **NOT** a protocol deviation.
- **What should I do if we obtain the blood sample outside of the sampling time window?**
 - **Answer: The data from this sample can still be used.** Record the actual time that the sample was collected on the PK blood collection eCRF and process and ship that sample as specified. While this is a procedural deviation, it is **NOT** a protocol deviation.



Frequently Asked Questions (Cont.)

- **What should I do if the volume of blood collected is less than 2.5 mL?**
 - **Answer:** The sample will still be used. Process and ship the sample as specified. This is NOT a protocol deviation.
- **What should I do if the blood sample is centrifuged greater than 2 hrs after sample collection?**
 - **Answer:** Record the procedural deviation under Question 8 of the PK blood collection eCRF. This is NOT a protocol deviation.
- **What happens if I have misplaced or damaged the sample kit?**
 - **Answer:** If pre-labeled vacutainer tubes or cryogenic vials are not available, you can use an EDTA-containing (lavender top) vacutainer tube for blood collection and a cryogenic vial or Eppendorf tube for the plasma sample available at your site. Tubes and vials should be labeled as specified in the Manual of Procedures.



Blood Collection Procedures

- Record the subject ID (4 digit code), sample ID, date, time, and drug infusion and PK sampling locations for each sample in the medical record, other appropriate source document, or directly in the ESETT PK eCRF.
 - If first recorded in another source document, transfer to the eCRF in WebDCU™ within 24 hrs of enrollment.
 - An example for drug infusion and blood sampling locations is right (or left) antecubital fossa (drug infusion) and right hand vein (PK sampling).
- Record any procedural deviations in the general comments section of the PK eCRF. Examples would be sample collected or processed outside of the specified time window.
- Samples collected outside of the sampling time windows or with smaller volumes than indicated are still useable and should be retained and shipped.

Blood Sample Processing

- **Within 2 hrs of the blood collection, separate plasma via centrifugation in the following manner:**
 - Centrifuge vacutainer tube for 10-20 minutes at 1000-2000 RCF at either room or refrigerated temperature.
 - Carefully aspirate the supernatant (plasma) taking care not to disrupt the cell layer.
- **Aliquot plasma into a labeled cryogenic vial and leave remaining pellet in vacutainer tube.**
- **Label the cryogenic vials and vacutainer tubes with the subject ID (4 digit code), time and date of blood collection.**

