Steps	Process	Numbers/resources
1. Screening and study entry		
1a. Check eligibility	In the following infants, start EEG, provide parent flyer and notify the neurology team: • HIE stage 2 or 3 • Any therapeutic hypothermia • Other encephalopathy, including meningitis • Suspected seizure, including unexplained apnoea • Moderate to severe metabolic acidosis (pH<7.0, base excess >12 mmol/L) and at risk of encephalopathy (discuss with SMO if EEG appropriate)	NeoLEV3 phone 09 6316128 The parent flyer is on the research trolley and the KFNC Research page
1b. Commence EEG	Commence EEG using 8 needle pattern as per KFNC EEG guideline (must insert temporal leads). Consider intranasal fentanyl for insertion and commence pain scores as per protocol. Consider IV analgesia (dexmedetomidine or morphine) depending on the pain scores and clinical context. Notify the study team when EEG running.	EEG guideline on KFNC Clinical Guidelines page
1c. Record eligibility	Print and complete the eligibility form	Research trolley or the KFNC Research page
1d. Facilitate neurology consent	Once the parent has read the flyer, ask if they would be willing to speak with a neurologist to find out more about the NeoLEV3 Study. Arrange for the NeoLEV3 neurologist to speak with the parents using their own phone or the ACNM phone. Provide Parent Information Sheet and Consent (PISC) form. Consent form must be countersigned by Neurologist or Chris McKinlay.	NeoLEV3 phone 09 6316128 Research trolley or the KFNC Research page
1e. Check baseline bloods	Ensure FBC, Cr, LFT have been tested within the last 24 hours	
2. Monitoring, initial treatment		
2a. Neurological monitoring	Neurologist monitors EEG. If neurological criteria are met (electrographic seizures for >30 s but <8 minutes per hour), the neurologist will ask for the first dose of levetiracetam to be given (60 mg/kg IV). If the seizure burden is high (≥8 minutes per hour) the infant is not eligible for NeoLEV3 and the neurologist will advise giving phenobaritone 20 mg/kg IV over 20 minutes (the baby is not eligible for levetiracetam as part of the NeoLEV3 Study).	Neurologist calls level 2 phone 021837261
2b. Levetiracetam first dose	If the neurologist advises giving the first dose of levetiracetam, administer **60 mg/kg IV over 5 minutes**. **Use dilution 15 mg/ml: take 3 ml of Levetiracetam 100 mg/ml and add to 17 ml of 0.9% NaCl so that 4 ml/kg = 60 mg/kg.** Record HR, RR, Sp02, BP before and after infusion on observation chart.	Neurologist calls level 2 phone 021837261
2c. Heart rate	Obtain an ECG rhythm strip from Mindray monitor after the infusion of 60 mg/kg levetiracetam. Go to the central monitor between bedspace 17 and 18 and select “freeze” and “print”. Date and time, and store with the clinical notes.	
3. Randomisation and trial intervention		
3a. Neurological monitoring	Neurologist continues to monitor EEG. If electrographic seizures are increasing or persist >30 minutes after commencing levetiracetam, the neurologist will randomise the infant into the dose escalation part of the study (3:1 ratio to either further levetiracetam 60 mg/kg IV over 5 min or phenobarbitone 20 mg/kg IV over 20 minutes). If the seizure burden is high (≥8 minutes per hour) the infant will not be randomised and the neurologist will advise giving phenobarbitone 20 mg/kg IV (study exit).	Neurologist calls level 2 phone 021837261

3b. Blood sample	Collect 0.6 ml plasma in an EDTA tube (lavender top) just before the second (dose escalation) levetiracetam dose. Send the blood sample to the lab using the **study request form**. **Do not send a hospital lab form.** Label tube with patient sticker and attach sticker to the request form. The **participant ID is the randomisation number**.	**Use the collection pack provided or download the request form from KFNC Research page**
3c. Dose escalation phase 2	Give levetiracetam 60 mg/kg IV over 5 minutes or phenobarbitone 20 mg/kg IV over 20 minutes **as advised by the neurologist according to the random allocation.** Record HR, RR, Sp02, BP before and after infusion If the infant is randomised to the levetiracetam dose escalation, have phenobarbitone available at the bedside (it does not need to be drawn up).	
3d. Blood sample	Collect 0.6 ml plasma in an EDTA tube (lavender top) 60-90 min after the second (dose escalation) levetiracetam dose. Send the blood sample to the lab using the **study request form**. This for the study only and consent has been obtained. **Do not send a hospital lab form.**	**Use the collection pack provided or download the request form from KFNC Research page**
3e. Heart rate	Obtain an ECG rhythm strip from Mindray monitor after the dose escalation of levetiracetam is given or after the phenobarbitone is given. Go to the central monitor between bedspace 17 and 18 and select “freeze” and “print”. Date and time, and store with the clinical notes.	
4. Post-randomisation care		
4a. Neurological monitoring	Neurologist continues to monitor EEG over the next hour. For those allocated to levetiracetam, if electrographic seizures do not resolve or recur within >60 minutes, the neurologist will advise giving phenobarbitone.	Neurologist calls level 2 phone 021837261
4b. Maintenance doses	The neurologist will advise if maintenance levetiracetam and/or phenobarbitone is required. • If levetiracetam controls the seizures by at least 50%, maintenance will be commenced for 5 days (20 mg/kg q8h IV or oral) • If seizures have been reduced by 50% but the infant is still seizing, they’ll receive levetiracetam maintenance and phenobarbitone load and maintenance for 5 days. • If seizures have not reduced by 50%, the infant will get a phenobarbitone load and maintenance for 5 days (levetiracetam discontinued). Levetiracetam maintenance 20 mg/kg 8-hourly (IV or PO) Phenobarbitone maintenance 5 mg/kg once daily (IV or PO)	Neurologist calls level 2 phone 021837261