WP-V : Clinical Trials

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WP-V Achievements in the Last 12 Months

- Creation of a collaborative consortium to support implementation of clinical trials *(ECET)*
- Identification of candidate treatments prioritized for testing in selected patient cohorts (EpiCARE deliverable)

European Collaboration for Epilepsy Trials (ECET)

- Consortium of investigators who share specific **expertise in the design and conduction of epilepsy trials** and agree to collaborate within the framework of Epilepsy Alliance Europe (EAE).
- **Main objectives:**
  - ✓ promote funding, design, implementation, analysis and reporting of high quality therapeutic trials in epilepsy
  - ✓ provide advice and professional expertise to any party involved in the conduction of clinical trials in epilepsy
  - ✓ implement educational activities aimed at improving the expertise of researchers and healthcare personnel involved in these
- Non-profit entity governed by ad hoc bylaws - EAE to serve as legal framework

List of candidate treatments to be prioritized for clinical trials - survey for EpiCARE members (17 institutions)

Key elements

- *Treatments targeting CNS immune-mediated and inflammatory mechanisms*
- *Precision treatments for rare syndromes, including gene therapies*
- *Cannabinoids*
- *Repurposing of treatments approved for other indications*

Candidate treatment	Target indication/population	Suggested trial design
ACTH (i.m.)	Continuous spike-wave in sleep (CSWS)	Steroids (oral)
Anakinra	Dravet syndrome (tonic-clonic seizure clusters)	Exploratory
Brivaracetam	Juvenile myoclonic epilepsy (JME)	Controlled versus valproate
Bromides	Dravet syndrome	Add-on controlled vs placebo
Cannabidiol	Angelman s. (myoclonic seizures)	Controlled add-on vs placebo
Cannabidiol	Hypothalamic amartoma	Exploratory
Cannabidiol	CSWS	
Cannabidiol	Focal seizures	Exploratory
Cannabidiol	Juvenile myoclonic epilepsy	Add-on controlled vs placebo
Cannabidiol	Ring chromosome 20 s.	Exploratory
Cannabidiol	Refractory epilepsy in adults	Controlled add-on vs placebo
Cannabidiol plus THC	Dravet and Lennox-Gastaut syndrome	Add-on controlled vs cannabidiol alone
Carbamazepine	Neonatal seizures	Exploratory
Disease modifiers (e.g. ASOs, gene therapy)	Dravet syndrome	Controlled (type of control to be discussed)
Everolimus (suggested by 3 responders)	Refractory focal epilepsy due to non-surgically treatable cortical dysplasia (e.g. type 2 FCD)	Exploratory or controlled add-on vs placebo
Everolimus (or other mTOR inhibitors) (2 suggestions)	Epilepsies related to mTOR pathway mutations	Controlled add-on vs placebo
Fenfluramine	Refractory epilepsy in adults	Controlled add-on vs placebo
Focused ultrasound	Hypothalamic hamartoma	Exploratory
Ketamine	Encephalopathy with refractory CSWS	Controlled add-on vs standard of care
Ketogenic diet	Eyelid myoclonias with absences	Controlled versus standard therapy (valproate, levetiracetam, ethosuximide)
Ketogenic diet	Ring chromosome 20 syndrome	Exploratory
Laser ablation guided by pre-study fMRI	Hypothalamic hamartoma	Controlled vs conventional laser ablation
Memantine	Epilepsy due to GRIN2A mutations	Exploratory
Micophenolate	Autoimmune (anti-GAD) epilepsy	Controlled vs standard therapy
Perampanel	Established status epilepticus	Exploratory
Perampanel	Progressive myoclonic epilepsies	Exploratory
Perampanel	Refractory absence seizures	Controlled, versus lamotrigine
Phenobarbital	Dravet syndrome (tonic-clonic seizure/clusters)	Controlled vs standard therapies
Quinidine (suggested by two respondents)	Epilepsy due to KCNT1 mutations	Exploratory or controlled vs placebo
Rituximab	Autoimmune (anti-NMDA) epilepsy	Controlled vs i.v. immunoglobulins
Stereotactic thermocoagulation	Hypothalamic hamartoma	Exploratory (compare outcomes from centers using alternative techniques)
Steroids	Unverricht-Lundborg syndrome	Exploratory
Steroids	Epilepsy due to limbic encephalitis	Controlled versus i.v. immunoglobulins
Steroids	Autoimmune epilepsies	Controlled vs IgG and/or other trearments
Topiramate	Dravet syndrome	Controlled versus standard therapy (valproate + clobazam + stiripentol)

Plans for next year

- Work on the list – feasibility of clustering for some proposals, further discussion on prioritization
- Follow-up on ongoing applications (quinidine, under C4C evaluation)
- Explore feasibility of spontaneous, low-cost trials replicating clinical practice
- Use Pillar 4 of EJP-RD for logistic help (accessible to ERNs)
- Prepare template protocol for trials in rare syndromes
- **Prepare to be competitive for coming calls:**
  - C4C calls (three letter of intent this year with Epicare members, anakinra /FIRES, quinidine/KCNT1, neonatal seizures)
  - Pillar 1 calls of EJP-RD for trials, to be launched in 2020

Use support from ECET

How to Contribute to Future Activities

- Respond to our requests in discussing priority lists
- Name a contact person for clinical trials and send it to us (Rima/Emilio cc Judit)
- Involve the network for collaborative trials, including ECET
- All requests and ideas are always welcome