



LIVERPOOL
**CLINICAL
TRIALS CENTRE**
LCTC

CLINICAL DIRECTORATE **NEWSLETTER**



*The Clinical Trials
Team at the
Liverpool Clinical*

International Clinical Trials Day

Clinical Trials Day is celebrated around the world on the 20th May to recognize the day that James Lind started what is often considered the first randomized clinical trial aboard a ship on May 20, 1747. This year, LCTC will be tweeting throughout the day about some of our recently completed and published trials. We will also be sharing tweets from our clinical trials staff who will be giving their perspectives on what clinical trials mean to them. Follow us on twitter @livuni_lctc. Our clinical trials website will also be posting news stories for the day at LCTC.org.uk.

On the 14th June 10:00-12:00 we will be hosting a virtual event via zoom in which there will be a series of presentations showcasing some of the trials within our portfolio, the development of the HEAL-COVID platform trial, and a newly developed application to predict, monitor, and reprofile recruitment. Everyone is welcome to join us and you can book on to the event via Eventbrite (<https://www.eventbrite.co.uk/>) and searching for Liverpool Clinical Trials Centre Celebrating Success.

Who we are and how to contact us

The Liverpool Clinical Trials Centre (LCTC) was formally launched in October 2019. We bring together a wealth of expertise built on the experience of the Clinical Trials Research Centre and the Liverpool Cancer Trials Unit, and have held full registration status with the UK Clinical Research Collaboration CTU network as the Liverpool Trials Collaborative since its establishment in 2007. To find out more about our clinical trials portfolio visit LCTC.org.uk where you can search our trials portfolio by trial stage, clinical area, or intervention type.

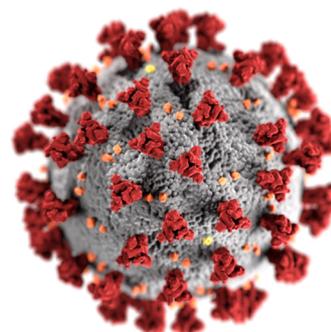
We receive core support from the University and infrastructure funding from the National Institute for Health Research which we use to support senior members of our team to collaborate with Chief Investigators on the development of new clinical trial ideas through to grant application. Successful development of a clinical trial grant application requires a multi-disciplinary approach and we provide expertise in statistics, trial management, data management and monitoring, information systems, quality assurance and regulatory affairs. If you would like to speak to us about collaborative opportunities then we can be contacted at lctc@liverpool.ac.uk or via the 'contact us' form on our website LCTC.org.uk. When we receive your message a senior member of the team will contact you to find out more about your plans. The time needed to work up a grant application shouldn't be underestimated so its best to contact us as early as possible.



Visit our website
lctc.org.uk

THE PANDEMIC AND CLINICAL TRIALS

Trial conduct has traditionally required staff to be present on a daily basis within the CTU. When the first lockdown hit this meant we rapidly needed to move over 100 staff to home working, change how we work and risk assess our trials portfolio. Like many we are yet to return to campus. We wanted to take this opportunity to thank our Chief Investigators and the whole of the LCTC team for their adaptability and continued efforts in facing the challenges in ensuring the safe conduct of our clinical trials during the pandemic.



While some clinical trials had to halt recruitment, this wasn't the case across our portfolio. Some trials were able to continue recruiting and others, although not open to new patients, had participants that needed to continue with their interventions and continue in follow up. In some of our trials, recruitment rates actually increased, possibly as a consequence of the societal value of research that was promoted during the pandemic.

Alongside our existing portfolio we also supported COVID-19 research. This included three observational studies looking at:

- transmission of COVID-19 within households (COVID-LIV);
- COVID-19 infection in cancer patients (CCP-Cancer);
- and contributing to ISARIC4C CCP-UK which aims to answer urgent questions about COVID-19;
- Conducting an analysis commissioned by the Deputy Chief Medical Officer to determine the safety and effectiveness of Remdesivir in the treatment of patients hospitalised with COVID-19.

Further information about these studies is available on our website. Finally we have been collaborating with researchers from Cambridge on a platform trial (HEAL-COVID) in the post-acute phase of COVID-19 which is now open to recruitment. For more information about HEAL-COVID follow @HEAL_COVID, go to our website heal-covid.net.



Neurology Trials

While the LCTC has its main trials portfolio areas in cancer and paediatrics it also has additional areas of strength which includes our neurological trials. This year has seen two of our neurology trials close and publish results:



NERVES is a randomised controlled trial to compare the clinical and cost effectiveness of transforaminal epidural steroid injection to surgical microdiscectomy for treatment of sciatica caused by a prolapsed intervertebral disc. The trial, funded by the National Institute for Health Research's Health Technology Assessment Programme sponsored by The Walton Centre NHS Foundation Trust started in 2014 was published in *Lancet Rheumatology* March 2021. The trial concluded that for patients with sciatica secondary to herniated lumbar disc, with symptom duration of up to 12 months, transforaminal epidural steroid injection be considered as a first invasive treatment option. Surgery is unlikely to be a cost-effective alternative to TFESI. For full publication see [https://doi.org/10.1016/S2665-9913\(21\)00036-9](https://doi.org/10.1016/S2665-9913(21)00036-9)

SANADII is a clinical trial designed to identify the most effective and cost-effective treatment for patients (adults and children over 5 years) with newly-diagnosed epilepsy. The trial, funded by the National Institute for Health Research's Health Technology Assessment Programme and sponsored by University of Liverpool and The Walton Centre for Neurology and Neurosurgery NHS foundation Trust conducted two un-blinded randomised controlled trials in parallel. The first (arm A) compared lamotrigine, levetiracetam and zonisamide in patients with a focal epilepsy, and the second (arm B) compared levetiracetam with valproate in patients with a generalized epilepsy or seizures that the clinician finds difficult to classify.



Arm A findings did not support the use of levetiracetam or zonisamide as first-line treatments for patients with focal epilepsy. Lamotrigine should remain a first-line treatment for patients with focal epilepsy and should be the standard treatment in future trials. Marson et al. *The Lancet*.10282 (2021): 1363-1374. [https://doi.org/10.1016/S0140-6736\(21\)00247-6](https://doi.org/10.1016/S0140-6736(21)00247-6)

Arm B found that compared with valproate, levetiracetam was found to be neither clinically effective nor cost-effective. full results see Marson et al *The Lancet*.10282 (2021): 1375-1386. [https://doi.org/10.1016/S0140-6736\(21\)00246-4](https://doi.org/10.1016/S0140-6736(21)00246-4)

Continuing the neurology trials portfolio we have two new trials starting later this year:

STOP EM: Surgeons Trial Of Prophylaxis for Epilepsy in seizure naïve patients with Meningioma: a randomised controlled trial. This trial aims to help adults diagnosed with a meningioma brain tumour that needs surgical removal and who have not had a seizure beforehand. We want to know whether a short course of an anti-epileptic drug (AED) started 1 day before surgery will prevent seizures happening after surgery. The study will run for about 6 years and is funded by the NIHR HTA. Working with the Chief Investigator, Professor Michael Jenkinson, Sir John Fisher Foundation / RCS Chair of Surgical Trials at the University of Liverpool, LCTC will begin trial development and setup later this year.

CRESCENT: Seizure control via pH manipulation: a phase II trial of inhaled carbogen adjunctive treatment of paediatric convulsive status epilepticus
This trial aims to help children who arrive in hospital Emergency Departments with an epileptic seizure that is not stopping. This is a medical emergency and is the commonest neurological emergency in children paediatric emergency departments. We want to know if we can stop seizures by altering brain acidity. In hospital, children with ongoing seizures are normally given 100% oxygen to breathe while they're getting other drugs. Carbon dioxide is very slightly

acidic: if you put a small amount into oxygen it makes the body (and brain) slightly acidic and this may help stop seizures. This mixture is called. It still has much more oxygen in it than room air (95% compared to 21%), and only the same amount of carbon dioxide as we normally breathe out.

In CRESCENT half the children would receive standard care treatment whilst breathing 100% oxygen (which is what happens now) and the other half would receive the same standard care whilst breathing (95% oxygen and 5% carbon dioxide). This trial will run for about 3 years and is funded by the NIHR EME. Chief Investigator is Dr Forsyth, from Newcastle Upon Tyne Hospitals.

Networking

LCTC benefits from and contributes to a number of networks that are working together to improve the landscape of clinical trial conduct. These networks include:

- UKCRC registered CTU network and its operational groups
 - Trial Managers Network
 - Clinical Data Managers
 - Trial Methodology Research Partnership
 - National Cancer Research Institute CTU group
 - Experimental Cancer Medicine Centres Network
- For many of these groups members of LCTC sit on executive committees or chair relevant subgroups contributing to strategic developments.