ENCHANTED News

Enhanced Control of Hypertension and Thrombolysis Stroke Study

August 2016

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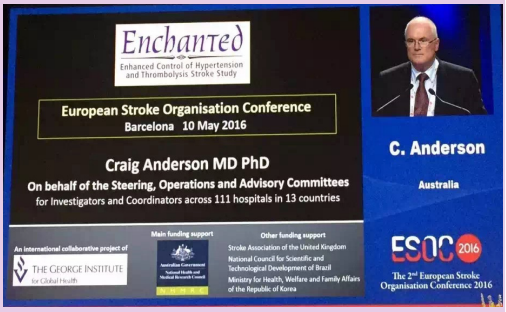


Prof. Craig Anderson on the big screen! Dr. Anderson and along with ENCHANTED collaborators revealed the findings of Arm A in Barcelona in May.

POINTS OF INTEREST

> Recruitment to begin in Malaysia. Congratulations to Hospital Kuala Lumpur for joining the ENCHANTED Study!

Arm B Recruitment Continues!!!

Keep Recruiting!!!

> Arm B of ENCHANTED trial still open and recruitment is still officially ongoing.

> Key Eligibility Criteria:

1. **Patients with acute ischaemic stroke for whom rt-PA thrombolysis is indicated and planned, no matter what dose**
2. **Baseline BP ≥ 150mmHg**
3. **Able to commence allocated treatment within 6 hours of stroke onset**

Brain imaging requirements for ENCHANTED

As a key secondary outcome for patients in ENCHANTED is the degree of symptomatic intracranial haemorrhage, you must order the correct MRI sequences if you opt to perform MRI rather than CT. To reliably detect haemorrhage we need a Gradient Echo sequence, often referred to as GRE or T2*. Without a T2* sequence, it can be difficult to adjudicate the presence or absence of haemorrhage. We also recommend you order a diffusion weighted imaging sequence as this allows us to determine whether the bleeding was within the infarct area. It can be surprisingly difficult to identify bleeding on the structural imaging sequences of T1, T2 or FLAIR.

Current Recruitment in ENCHANTED BP Arm

As of 1 August 2016, **1281** patients have been enrolled in the BP Arm. This leaves only 1023 to go.

Message from Professor Richard Lindley

Honorary Professional Fellow, Neurological & Mental Health Division (Injury, Frailty and Disability)

Thank you to all of you who randomised a patient last month. Our total recruitment of blood pressure arm by 1st August was 1,281 participants, over half way to our recruitment target of 2,304. To achieve this target we will need to double our recruitment rate so we are encouraging all active sites to screen as actively as possible in order not to miss a patient. For those of you who have not recruited recently, please review your local research plans and consider prioritising ENCHANTED.

ENCHANTED asks a really important question, and one that clinicians have been asking ever since thrombolysis became a routine treatment, what should we do about blood pressure? The recent observational data from IST-3 (reviewed in previous newsletters) supported BP lowering but we now need data from a randomised controlled trial to confirm this promising intervention (Stroke 2015; 46: 3362-3369).

To remind you, these are our key eligibility criteria:

- Will or has received rt-PA (local dose protocol)
- BP $\geq$150mmHg and $\leq$ 185mmHg
- No definite indication or contraindication to intensive BP lowering (i.e. appears feasible with no clear hazards for that patient)
- BP lowering can commence within 6 hours of stroke onset

The 6-hour time window allows you to start rt-PA treatment and then consent potential eligible patients, so this will not increase your door-to-needle times, so crucial for many of you.

Whilst we seek increased recruitment, we also want good data. And experience has provided a few simple tips for BP management. If you need to pre-treat patients with severe hypertension to achieve rt-PA eligibility (e.g. treating arrival BPs over 185mmHg to get the patient below 185mmHg for safe thrombolysis), consider using a GTN patch or infusion.

Once the BP is under 185mmHg you can then safely treat with rt-PA, and you can then assess for ENCHANTED. If the BP is within our trial eligibility (150 to 185mmHg), you can consent and randomise. The GTN patch or infusion should be stopped once the trial consent is obtained.

Remember, our key secondary outcome measures are symptomatic intracranial haemorrhage (sICH), so you must order a GRE (T2* or equivalent) if using MRI for follow-up so the central adjudicators can make a reliable assessment of the extent, if any, of any sICH.

Conference Update

ENCHANTED rtPa arm results at the EUROPEAN Stroke Organisation Conference (ESOC) in Barcelona

The ENCHANTED results for the rTPA arm were announced at the 2nd ESOC in Barcelona on 10 May 2016. The conference was attended by 3,700 delegates and the presentations were in the auditorium with the main official opening session. The main results were present in a trio and closely followed by two other presentations on the next days, which created a huge hype throughout the whole conference.

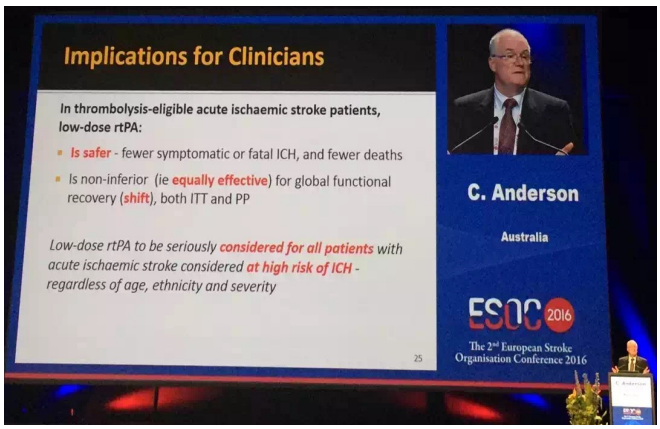
Lots of congratulations and positive feedback were received. There were several media present and interviews conducted with Professor Anderson and others. The next day the results were splashed across several newspapers around the world and in several languages, with various headlines such as, "Reduced dosage clot busting drug can improve Stroke treatment" (WashingtonNewsWire.com) "International study reveals clot busting drugs are safer in lower dosage" (Channel Nine News Australia) and "Lower dose of tpa found safer for patients with acute ischaemic stroke" (MedicalResearch.com).

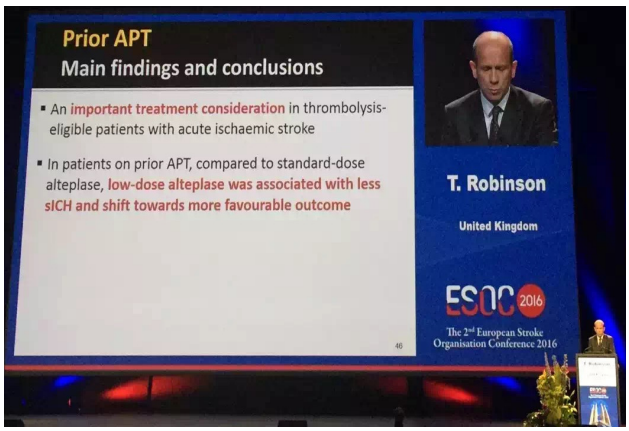
The trio presented continuously were:

- "ENCHANTED main results – Trial of low-dose versus standard dose intravenous tissue plasminogen activator in 3310 patients with Acute Ischaemic Stroke" by Professor C. Anderson
- "Efficacy of low dose vs standard dose rtPa between Asian and non-Asian with particular emphasis on stroke subtype and risk of intracerebral haemorrhage" by Professor J. Chalmers
- " Benefits and risks of low versus standard dose Alteplase in patients on prior antiplatelet therapy: The ENCHANTED Trial" by T. Robinson

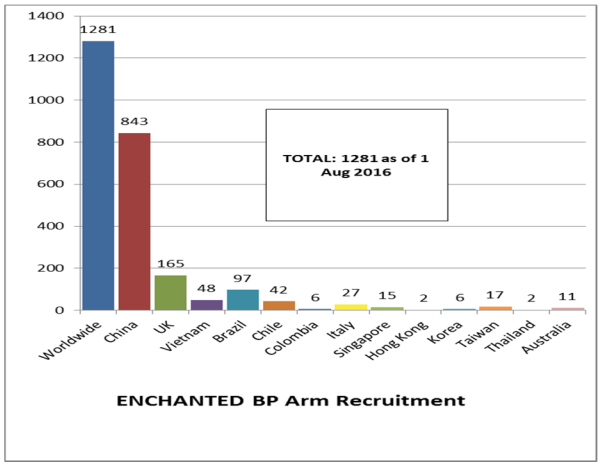
On the next day, 11th May, the two presentations presented were:

- "rtPa dose relevance to older patients" by Professor R. Lindley
- "rtPa dose in the context of endovascular clot retrieval" by Professor J.S. Kim



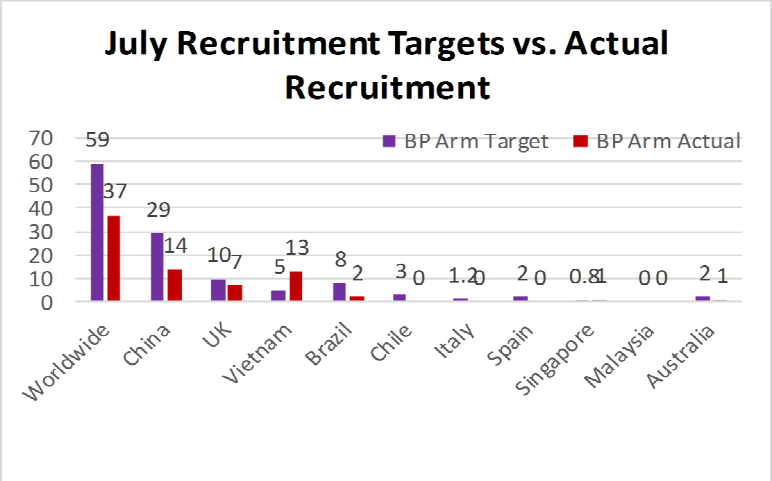


Recruitment and site performance data



1023 to go!

Total of 38 patients recruited in July!



TOP 5 RECRUITING SITES : JULY 2016

Centre	Country	Total
The People's Hospital 115	China	8
Xuzhou Central Hospital	China	5
Kings College Hospital NHS Foundation Trust	UK	3
1st affiliated Hospital of Baotou Medical College	China	3
Bach Mai Hospital	Vietnam	3

Recruitment Targets for August

Country	Target
China	29
UK	10
Vietnam	5
Brazil	7
Singapore	0.5
Chile	2
Italy	1.5
Australia	2
TOTAL	**57**

Brain imaging collection rates as of 3rd August 2016

Country	Patients enrolled	Discrepancy between IS and DB*	Patients with all scans uploaded	Rate of scan upload
Worldwide	**343**	**15**	**214**	**62.4%**
Chile	2	0	2	100.0%
Italy	7	0	7	100.0%
Singapore	7	0	6	85.7%
United King-dom	102	11	65	63.7%
China	169	4	101	59.8%
Brazil	22	0	13	59.1%
Australia	2	0	1	50.0%
Vietnam	24	0	11	45.8%

CRF completion rates as of 11th August 2016

	Expected complete patients	Complete eCRF in Study Database	Complete Patient Data Rate	Outstanding Day 90
Worldwide	1189	1104	93%	52
Italy	25	25	100%	2
Singapore	12	12	100%	0
Chile	42	41	98%	0
Vietnam	26	25	96%	2
China	807	759	94%	37
Brazil	91	85	93%	1
Australia	10	9	90%	0
UK	143	115	80%	10

ICC Employee Profile: Leibo Liu

Title: Clinical Trials Assistant
From: Beijing, China
Studies: ENCHANTED, HEADPOST, FABRY, HAPPY

Leibo serves as the Clinical Trials Assistant for ENCHANTED. He has been with The George Institute since 2014. With a background in software engineering Leibo was a added to the ENCHANTED team to help with many Information Technology.

His various responsibilities for ENCHANTED include creation of two very important recurring reports: the Operations Report and ICC Monthly Report. In addition, Leibo handles much of the Data Management overseeing the website, the database and Mistar, the Image Server used for brain scans.

Leibo's favourite part of working on ENCHANTED is the large scale of the study which allows him to get valuable experience in data management and software engineering.

While ENCHANTED work is his largest responsibility, Leibo also contributes to the HEADPOST study and is helping with the genesis of both the FABRY and HAPPY projects.