Data highlights from the opening plenary of ESOC 2017

by ESO | 16.5.2017 | Kategorie 1 | 0 comments

Data highlights from the opening plenary of ESOC 2017

MEDIA RELEASE

- DAWN study – mechanical thrombectomy between 6 and 24 hours from symptom onset significantly prevented disability in patients with severe strokes and 'mismatch' on brain imaging.
- CLOSE and Gore-REDUCE – PFO closure significantly reduces recurrent stroke in younger adults with cryptogenic stroke.
- PICASSO study – Probucol significantly reduces recurrent cardiovascular events in ischemic stroke patients with a high risk of cerebral haemorrhage.
- NOR-TEST study – No significant difference in functional outcome between acute stroke patients who received standard of care, alteplase, and those who received tenecteplase.
- Other highlights came from RATS-3 (benefit of early intensive cognitive linguistic therapy), T3 (nurse-initiated intervention to reduce disability) and ASTER (contact aspiration versus stent retriever).

See video interviews with principle investigators and summary slides at: **http://www.esoc2017.com/conference-information/conference-news**

Prague, 16 May 2017 – Presentations during the opening session of the 3rd European Stroke Organisation Conference (ESCO) 2017 offered an encouraging mix of positive results and useful data. From the success of the CLOSE and REDUCE trials showing benefit of PFO closure, to the DAWN trial which expands the population of patients who will benefit from thrombectomy, to the PICASSO study in secondary prevention of stroke, there was plenty of fuel for discussion and debate. In only its third year, ESOC has strengthened its reputation as Europe's premier stroke conference with teaching courses and presentation of results from major clinical trials. Highlights from the morning plenary are outlined below.

Holes in the Heart: To close or not to close?

Two trials aimed to answer the ongoing controversy of whether or not closing a patent foramen ovale (PFO, a small hole in the heart which affects 20-25% of the population) reduces the risk of recurrent stroke in patients with a stroke of unknown origin.

In the **CLOSE Study**, closure of a high-risk PFO was associated with a significantly lower rate of recurrent stroke in patients with a PFO who had experienced a cryptogenic stroke. These results were presented by the Principal Investigator Prof Jean-Louis Mas of the Hôpital Sainte-Anne, Paris, France. This academically-driven, multicentre study (32 study sites in France and 2 sites in Germany) compared whether endovascular closure of PFO reduced the risk of recurrent strokes compared to blood thinning drugs alone. It included 663 patients who had experienced a stroke of unknown origin.

Key findings from the CLOSE study:

- PFO closure significantly reduced the risk of recurrent stroke compared to anti-platelet therapy (HR 0.03, 95% CI 0 to 0.25, p < 0.001).
- The difference in risk of recurrent stroke with anticoagulants vs. anti-platelet therapy was not significant (HR 0.43, 95% CI 0.1 to 1.5, p=0.17).
- There was an increased risk of atrial fibrillation with PFO closure, mostly periprocedural and of uncertain significance.

"These data will change clinical practice in patients with cryptogenic stroke with atrial septal aneurysm or a large shunt," said Prof Mas. "I also believe the question of whether or not to close a PFO in this subset of patients has been answered by these data – the answer is yes."

In the **Gore-REDUCE Study**, closure of a PFO with a GORE® Helex® or or GORE® CARDIOFORM Septal Occluder

device was associated with a significant reduction in risk of recurrent stroke in adults with PFO and cryptogenic stroke. Principal Investigator Prof Scott Kasner of the University of Pennsylvania, Philadelphia, US, presented the findings of this study. PFO closure reduced risk of recurrent strokes in 664 patients across 63 centres in 7 countries, with a previous stroke of unknown origin.

Key findings from the Gore-REDUCE study:

- The study achieved statistical significance with both its primary endpoints with a 77% relative reduction in clinical stroke hazard and a 49% relative risk reduction in new brain infarction.
    - PFO closure with a GORE® HELEX® or CARDIOFORM® device was associated with a reduction in recurrent clinically apparent stroke (HR 0.23, 95% CI 0.09-0.62, p=0.001) and silent ischaemia on brain imaging (RR 0.51, 95% CI 0.29 to 0.91, p=0.024).
- There was a small increase in the periprocedural risk of atrial fibrillation (6.6% vs 0.4%, p<0.001).
- Effective closure was achieved in 94.5% of patients.

"In carefully selected patients with cryptogenic stroke, PFO closure with GORE devices significantly reduced the risk of recurrent stroke… with a number needed to treat of 28 over 2 years," said Dr Kasner. "These data provide clear and definitive evidence that PFO closure is beneficial in this patient population."

CLOSE and Gore-REDUCE are the first studies to independently show benefit from endovascular closure of higher-risk PFOs, associated with a moderate shunt or and atrial septal aneurysm. This has the potential to significantly change clinical practice for a large population of patients in whom an inability to define the cause of their stroke left them without a specific treatment option.

Mechanical thrombectomy: Widening the window?

In the **DAWN Study**, mechanical thrombectomy in patients presenting late (after the standard 6 hours but before 24hrs) or who woke with symptoms reduces disability.

An independent Data Safety Monitoring Board (DSMB) recommended that the study be stopped early based on a pre-planned interim review of data from the first 200 patients (of a planned 500). The review concluded that multiple pre-specified stopping criteria were met. Joint Principal Investigators Dr Tudor Jovin of the University of Pittsburgh School of Medicine and Dr Raul Nogueira from Emory University School of Medicine, USA, presented the data at ESOC 2017 today.

The DAWN study sought to answer whether advanced imaging methods with MRI DWI and CT-perfusion can be used to successfully select patients for endovascular therapy, even though they present late or have an uncertain onset of symptoms. They included patients in whom brain imaging demonstrated a significant area of potentially salvageable brain tissue. Endovascular treatment significantly reduced disability compared to medically managed patients.

Key findings from the DAWN study:

- There was a significant relative risk reduction (73%) in disability in 107 patients receiving mechanical thrombectomy compared to 99 with medical management (OR 2.1, 95% 1.20 – 3.12, p<0.001), with a number needed to treat of 2.8 to reduce disability.
- There was a 35% increase good functional outcome defined as mRS score of 0-2.
- There was no significant difference in safety outcomes between groups.

“This study shows that for every 100 patients treated with endovascular therapy, 49 will have a less disabled outcome as a result of treatment, including 36 who will be functionally independent,” said Dr Jovin. “These results greatly expand the population of patients who can significantly benefit from mechanical thrombectomy for stroke, to significantly reduce severe functional impairment in the mostly severely affected patients. However, the shorter the time frame to treatment, the better the outcome, so the mantra ‘time is brain’ still stands.”

In the **PICASSO trial,** the lipid-lowering and anti-oxidant drug probucol significantly reduced recurrent cardiovascular events in patients with ischaemic stroke and a high risk of cerebral haemorrhage. The principal investigators, Prof Sun U Kwon and Prof Eun-Jae Lee of the Asan Medical Center, Seoul, Republic of Korea presented study results at ESOC 2017 today.

The PICASSO trial was a 2 by 2 factorial randomised trial of cilostazol or probucol compared to placebo in 1512 patients with a non-cardioembolic ischaemic stroke or TIA at an increased risk of intracerebral haemorrhage due to previous haemorrhage or multiple microhaemorrhages on brain imaging.

Key findings from the PICASSO study:

- The primary efficacy endpoint of stroke, myocardial infarction or cardiovascular death was significantly reduced by probucol (HR 0.69 (95% CI, 0.50–0.97), p = 0.031).
- There was no significant difference in the primary safety endpoint of recurrent cerebral haemorrhage.

In this population, probucol significantly reduced the risk of recurrent cardiovascular events, offering a potential new treatment for secondary prevention of ischaemic stroke in patients at an increased risk of cerebral haemorrhage. Although this requires confirmation in other clinical populations, it offers an exciting new treatment approach in these difficult patients at risk of both major forms of stroke.

“Probucol treatment in addition to standard lipid regimen may be more efficacious than standard lipid treatment, although more further research is needed,” commented Prof Lee.

A new clot-buster for acute stroke?

In the **NOR-TEST study**, a new clot-buster (tenecteplase) was compared to standard treatment (alteplase) after acute stroke. Dr Nicola Logallo, Haukeland University Hospital, Neurology, Bergen, Norway presented the findings at ESOC 2017 today.

Alteplase is the standard clot-busting drug used for intravenous thrombolysis up to 4.5 hours after onset of an ischaemic stroke. The NOR-TEST study compared standard treatment with alteplase with 0.4mg/Kg of the newer clot-busting drug tenecteplase in 1100 patients with acute ischaemic stroke.

Key findings from the NOR-TEST study:

- There was no significant difference between groups in disability at 3 months (mRS 0-2).
- There was no significant difference in rates of symptomatic intracerebral haemorrhage.

“Based on these findings, physicians may choose to use tenectaplase because of its convenience,” commented Dr Logallo. “Its single administration is easier and you can be sure the patient gets the full dose”.

In the **RATS-3 study,** intensive cognitive linguistic therapy was not beneficial in most patients early after acute stroke. Prof Femke Nouwens, Speech and Language Therapist, Erasmus Medical Centre, The Netherlands presented the findings.

Aphasia remains one of the most significant causes of disability after stroke and there are few effective treatments. Early intensive cognitive linguistic therapy (CLT) is a potential novel treatment. Prof Nouwens reported the results of the RATS-3 trial, testing whether intensive CLT within 4 weeks after stroke in 152 patients was effective.

Key findings from the RATS-3 study:

- Only 29% of patients in the intervention group were able to receive the targeted amount of therapy
- There was no significant difference in language function between groups with no clinically or statistically significant difference between treatment groups.

"In this population, early intensive CLT was neither feasible or effective for the majority of patients," concluded Prof Nouwens.

In the **T3 study**, a nurse-initiated, evidence-based care bundle to improve Triage, Treatment and Transfer of acute stroke patients did not reduce disability at 90 days. Prof Sandy Middleton, Australian Catholic University, Nursing Research Institute, Sydney, Australia presented the results at ESOC 2017 today. The study included 1879 participants in 26 Australian Emergency Departments.

Key findings from the T3 study:

- There was no significant difference between groups for the primary outcome of 90-day modified Rankin Scale score.
- There was no significant difference between groups for 11 secondary quality of care outcomes.

The care bundle did not significantly affect outcomes in this population and there was no evidence of a significant impact on quality of care delivered in Australian Emergency Departments.

Are there alternative methods of mechanical clot removal for acute ischaemic stroke?

From the **ASTER study,** Professor Lapergue from the Foch Hospital, University of Versaille, France, reported that there was no significant difference in safety or efficacy with contact aspiration compared to the standard method of mechanical stent retriever for clot retrieval after acute stroke, demonstrating its as potential as an alternative treatment approach.

Key findings from the ASTER study:

- There was no significant difference between groups for the primary outcome of 3 month mRS OR for 1 point improvement (0.76, 95%CI 0.53 – 1.10, p=0.15).
- Rates of reperfusion were similar in the intervention group (TICI 2b/3 85.4% vs 83.1%).

The ASTER trial demonstrated no significant difference between the current accepted method of clot retrieval in acute stroke and the new method of contact aspiration. Further research will be required to help us decide which approach to use.

"The ASTER trial opens the door to add a new tool (ADAPT) to remove clots," commented Prof Lapergue. "We have reached a milestone in terms of strategic approach."

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Menu

About ESO
Membership
Meetings
Projects
Resources & Education
Publications

Information

Contact
Career
Events
News
Support ESO

Afternoon Highlights from ESOC 2017

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Highlights from the first afternoon of ESOC 2017

MEDIA RELEASE

- ESO-SAFE partnership is launched with the release of the Burden of Stroke Report, and a report on policy, access and quality of care.
- VISTA Collaborators: The benefits of thrombectomy are confirmed and the importance of rapid treatment emphasised.
- HERMES Collaborators: The benefits of mechanical thrombectomy for acute ischaemic stroke are greater with smaller ischaemic core but it remains effective with increasing volume.
- TO-ACT Study: No significant benefit from endovascular treatment in severe cerebral venous sinus thrombosis.
- TALOS Study: Further research of SSRIs is required to assess benefit after ischaemic stroke.
- TESPI Study: Findings support thrombolysis for acute ischaemic stroke in patients over 80 years of age.

***See video interviews with principal investigators and summary slides at*: http://www.esoc2017.com/conference-information/conference-news.**

Prague, 16 May 2017 – Attendance at the third European Stroke Organisation Conference (ESOC) outstripped demand for space in the opening plenary as more than 4,000 delegates gathered in Prague for three days of the latest clinical study results, teaching courses and practical training. Excitement generated by the scientific programme continued into the afternoon with further data announcements, as well as the launch of the new partnership between the European Stroke Organisation and the Stroke Alliance For Europe (ESO-SAFE). Highlights from the afternoon's scientific programme are outlined below.

Launch of the Action Plan for Stroke in Europe 2018-2030, ESO-SAFE Memorandum of Understanding and Burden of Stroke Report

The Memorandum of Understanding between the European Stroke Organisation and the Stroke Alliance for Europe, cements a partnership between the leading European professional and patient organisations. The first act was to launch the Burden of Stroke Report, providing the most accurate, up to date record of the incidence, prevalence and outcomes from stroke as well as a report on policy, healthcare infrastructure, service provision and quality related to stroke treatment. These initiatives are important steps in the development of the Action Plan for Stroke in Europe 2018 to 2030. This will guide European Union policy on research and management of stroke for the next decade.

Note: A video interview with Prof Bo Norrving, leader of this initiative, will be available from 18:00 CET on Wednesday 17 May at at: http://www.esoc2017.com/conference-information/conference-news.

Modifiers of Endovascular Treatment Effect and Importance of Time Delays

Mechanical thrombectomy has revolutionised the treatment of large vessel ischaemic stroke. In the largest study of its kind, the factors which modify the efficacy of this treatment were assessed by the Virtual International Stroke Trials Archive (VISTA) Collaborators. Principal investigators, Prof Pooja Khatri (University of Cincinnati, USA) and Prof Diederik Dippel (Erasmus University Medical Center, Rotterdam, The Netherlands) presented an analysis of data from 14 studies.

Key findings presented by Professor Khatri:

- The odds ratio for improved disability was 1.94 (95% CI 1.6 to 2.39) with endovascular treatment compared to control.
- There was no significant difference in mortality.
- Age did not modify the effect of treatment but older age was associated with worse outcome in both groups.

Key findings presented by Prof Dippel:

- There was a significant relationship between time from onset to groin puncture and efficacy of thrombectomy.
- There was a significant relationship between time from onset to reperfusion and efficacy of thrombectomy.

“The evidence for endovascular therapy is robust, even if we include the prior negative trials,” said Khatri. “For a one hour delay the absolute reduction in likelihood of a good functional outcome is 9.5%,” added Prof Dippel.

Prognostic and Treatment Impact of Penumbral Imaging

Data from the ground-breaking HERMES Collaboration of the thrombectomy randomised studies has been used to assess the effects of CT-perfusion imaging on predicting the benefit from mechanical thrombectomy for acute ischaemic stroke due to large vessel occlusion. On behalf of the HERMES Collaborators, principal investigator Prof Bruce Campbell (Royal Melbourne Hospital and The University of Melbourne, Australia) presented findings from an assessment of the modified Rankin Scale (mRS) scores at 90 days in 900 patients.

Key findings:

- Ischaemic core size on CT-perfusion and MRI were independently associated with functional outcome but did not modify the effect of treatment
- Despite poorer outcome, endovascular intervention was still beneficial in patients with larger ischaemic cores, up to at least 70mls. Beyond this, benefit was uncertain.

“The number of patients needed to treat (with mechanical thrombectomy) to achieve good outcome tends to increase with estimated ischaemic core volume,” commented Prof Campbell. “However, overall point estimates remain at levels that may be worthwhile at higher estimated core volumes.”

These data should help to guide patient selection for thrombectomy.

TO-ACT Study: Endovascular Treatment in Severe Cerebral Venous Sinus Thrombosis

Cerebral venous thrombosis is a rare cause of stroke and the optimal management in severe cases is unclear. Principal investigator Prof Jonathan Coutinho (Academisch Medisch Centrum, Amsterdam, The Netherlands) presented the first results from the TO-ACT study in 63 patients with severe CVT, randomised to endovascular treatment with thrombolysis and/or mechanical thrombectomy, or anticoagulation alone. The primary outcome was mRS score at 12 months. The trial was stopped at the first interim analysis for futility.

Key findings of the TO-ACT study:

- Endovascular treatment does not alter outcomes in severe cerebral venous sinus thrombosis.
    - There was no significant difference in mRS scores between groups (OR 0.95, 0.34-2.68).

This small study demonstrated no significant benefit from endovascular treatment in severe CVT.

TALOS Study: Potential Benefit of Selective Serotonin Reuptake Inhibitors (SSRIs) After Acute Ischaemic Stroke

Previous studies have demonstrated a possible benefit from antidepressant drugs called SSRIs after acute ischaemic stroke. Principal investigator Prof Kristian Kraglund (Aarhus University Hospital, Denmark) presented the initial findings of the TALOS study in which 642 patients with acute ischaemic stroke were randomised to receive citalopram or placebo.

Key findings from the TALOS study:

- Citalopram was safe in ischaemic stroke.
- There was a no significant benefit from citalopram in improving functional status (OR for mRS improvement 1.27, 0.92-1.74, p=0.14).
- There was no difference in rate of recurrent vascular events.

This study shows that further research is required before SSRIs can be used in stroke rehabilitation. “Although we have shown that treatment with citalopram was safe,” said Prof Kraglund. “It is not yet time to recommend the use of SSRIs after stroke in patients without depression.”

TESPI Study : First Dedicated Study of the Benefit of Intravenous Thrombolysis in Patients >80 Years of Age

Treatment with intravenous alteplase for acute ischaemic stroke (thrombolysis) has been the standard of care for more than 20 years, but there has not yet been a dedicated study in patients over 80 years of age. Co-principal investigator Prof Svetlana Lorenzano (Acute Stroke Unit, Policlinico Umberto Hospital, Rome, Italy) presented the results of the TESPI trial in patients over 80 years of age, within 3 years of onset. Despite early cessation of the study, there was a trend towards benefit in this patient group consistent with findings from studies in younger patients and subgroups of patients over the age of 80 included in other studies.

Key findings from the TESPI study:

- There was a non-significant increase in patients with a good functional outcome measured using the mRS with alteplase (mRS 0-2: OR 1.35, 0.69-2.64)
- There was no increase in rates of symptomatic intracerebral haemorrhage with alteplase.

These findings, in the light of similar results from other studies, support the use of alteplase in this age group. “If we compare these data with those from previous trials, the results of thrombosis within three hours in elderly patients are similar to those reported in younger patients,” said Prof Lorenzano.

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Menu

About ESO
Membership
Meetings
Projects
Resources & Education
Publications

Information

Contact
Career
Events
News
Support ESO

Cerebral Small Vessel Disease – ESOC 2017 Session Highlights

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The small vessel disease (SVD) session covered a broad spectrum, from animal models over disease mechanisms, neuroimaging to treatment. The session was enriched by questions from the audience using the "ask the expert" function within the ESOC smartphone app.

Eric Jouvent summarized imaging findings in SVD and addressed questions that frequently come up in clinical routine, such as differential diagnosis. He emphasized the importance to integrate information from different MRI contrasts. While very small acute lesions can be difficult to detect, follow-up imaging might provide additional information.

Joanna Wardlaw and Marco Duering discussed the role of blood-brain-barrier (BBB) dysfunction in SVD. Human studies *in vivo* (in particular dynamic contrast enhanced MRI) and post-mortem histopathological analyses suggest increased BBB leakage with aging and in association with SVD. However, some studies are conflicting. Animal models also support a role of BBB failure in SVD: CADASIL transgenic mice show a reduced pericyte coverage and extravasation of plasma proteins. BBB leakage has also been found in *Foxf2*-knockout mice and *FOXF2* has recently been linked to SVD in a genome-wide association study.

Andrew Lawrence focused on network dysfunction in SVD. Structural networks are based on MRI tractography and can be characterized by measures from graph theory, such as global efficiency. These network measures are strongly related to cognitive symptoms in SVD, both in cross-sectional and longitudinal studies. Interestingly, the effects of other SVD markers on cognitive symptoms are largely mediated by network measures, suggesting that network dysfunction might be a common pathway for different SVD-related lesions.

Andy Shih provided fascinating insights on cerebral microinfarcts using rodent models. Cortical microinfarcts can be well modelled and investigated, e.g. using *in vivo* 2-photon microscopy. Interestingly, microinfarcts cause clinical symptoms that extend beyond the infarct core and originate from perilesional tissue. Microinfarcts may even cause effects remote from the lesion site, e.g. in connected regions, and this will be investigated in future studies.

Hugh Markus summarized the treatment of SVD patients. He emphasized that we have limited knowledge from clinical trials and therefore a great demand for new trials. In addition, there is a need for better stroke subtyping in large stroke trials as many classification systems cannot discriminate between SVD-related infarcts and small infarcts of other etiology. Some specific recommendations: Double platelet inhibition should be avoided, also in the acute phase. Recent data from an Austrian registry suggest that thrombolysis is equally beneficial in SVD-related stroke compared with other stroke subtypes. Antihypertensive treatment is very important, also in SVD patients without stroke. But blood pressure lowering might be harmful in late disease stages, as it can augment hypoperfusion. Ultimately, a better understanding of SVD pathomechanisms is needed in order to develop new therapies.

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Menu

About ESO
Membership
Meetings
Projects
Resources & Education
Publications

Information

Contact
Career
Events
News
Support ESO

Stroke in the Young – Session Highlights from ESOC 2017

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This interesting session, Chaired by M. Steinlin and J. Putaala, covered the most relevant areas of cerebrovascular disease in the young age, pointing out well calibrated updates on selected topics and take-home messages oriented to the clinical practice.

First speaker of the session, Dr. Annette Fromm from Bergen (Norway) showed a complete overview of diagnostic pathways in young stroke patients, following literature proposals and the experience of the ongoing NOR-SYS study, addressing in particular this item, with a special focus on under evaluated role of "classical" vascular risk factors in young people and sub-clinical atherosclerosis with a systemic screening screening approach.

The second speaker, L. Rutten-Jacobs, pointed out the consequences of this underestimation of traditional vascular risk factors in young people with stroke, using the results of FUTURE study and showing us the complex but non favourable long term outcome of TIA/stroke in young people mostly regarding stroke recurrence, cognitive consequences, loss of quality of life, unemployment rate and so on.

The other speakers, D.d.A.D. de Sousa, A. Singhal, and F. Heinen, gave us a significant update about new evidence and active research fields about:

– cerebral venous thrombosis, whose epidemiology, diagnosis, risk factors and treatment are changing or more deeply investigated

– reversible cerebral vasoconstriction syndrome and the overlapping phenotype and pathophysiology with thunderclap headache and primary central nervous system vasculitis

– pediatric stroke pathways, presenting a standardized management plan and showing the difficult differential diagnosis of cerebrovascular disease in children.

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About ESO
Membership
Meetings
Projects
Resources & Education
Publications

Information

Contact
Career
Events
News
Support ESO

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3rd European Stroke Organisation Conference: late breaking abstracts

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CLINICAL TRIAL RESULTS – ACUTE MANAGEMENT – THROMBOLYSIS OR THROMBECTOMY

GENERAL OR LOCAL ANESTHESIA IN INTRA ARTERIAL THERAPY ("GOLIATH"): A RANDOMIZED TRIAL

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Background and Aims: Endovascular therapy (EVT) is now evidence based. There is uncertainty regarding the effect of the anesthetic approach. Observational studies suggest that general anesthesia (GA) during EVT is associated with worse outcomes compared to conscious sedation (CS).

We aimed to examine whether GA caused greater infarct growth and worse outcomes during EVT by randomizing patients to either GA or CS. Patients were MRI scanned before and 48–72 hours after EVT. Patients were contacted by an independent observer 90 days post-stroke to asses the modified Rankin scale (mRS).

Method:

Inclusion criteria

- anterior circulation large vessel stroke
- 6 hour time window
- mRS 0–2
- presenting infarct volume <70 cc
- Not intubated at arrival/Glasgow Coma Scale>8

Results: A total of 128 patients were included in the study. Sixty-two were randomized to CS; four were converted to GA. (Conversion rate 6%). Analysis was done by "intention to treat".

The two groups were balanced (Table 1). The GA group took approximately 9 minutes longer to prepare for EVT. Significantly more patients in the GA group experienced a drop in blood pressure. Results concerning infarct growth and 90 day mRS will be presented at the conference.

Table 1: For categorical values, a Chi-square test was performed. Age and time to groin were normally distributed and mean and standard deviation are presented. For the other continuous variables, a Mann-Whitney test was done. Median and interquartile ranges are shown.

	General anesthesia n=66	Conscious sedation n=62	p-value
Age	70.5 (10.5)	72.3 (12.3)	0.21
Women	30 (45%)	32 (52%)	0.49
NIHSS	17.5 (13-21)	17.5 (15-21)	0.81
Hypertension	39 (59%)	32 (52%)	0.44
Atrial fibrillation	24 (36%)	27 (44%)	0.39
Diabetes	10 (15%)	8 (13%)	0.55
Smokers	21 (32%)	19 (31%)	0.34
Lesion			
ICA-neck	6 (9%)	2 (3%)	0.17
ICA-T	8 (12%)	11 (18%)	0.37
M1	22 (33%)	31 (50%)	0.06
M2	7 (11%)	12 (19%)	0.28
Tandem	18 (27%)	11 (18%)	0.20
Symptom onset to admission at comprehensive stroke center (min)	103.5 (66-200)	98.5 (54-177)	0.42
Symptom onset to groin (min)	203.3 (71.6)	183.9 (71.0)	0.13
mTICI 2b-3	55 (83%)	45 (73%)	0.14
Time from groin to reperfusion (min)	37 (21.75-50.75)	30 (19.75-55.5)	0.69
Symptom onset to reperfusion (min)	213 (187-294.5)	207.5 (161-280)	0.27
Time from arrival at intervention room to groin (min)	24 (20-27)	15 (12-19)	<0.0001
Numbers of patients with a 20% drop in MAP	57 (86%)	22 (35%)	<0.0001

Conclusion: The results from this study may guide future decisions regarding the optimal anesthetic regime for EVT.

LB01-003

CLINICAL TRIAL RESULTS – ACUTE MANAGEMENT – THROMBOLYSIS OR THROMBECTOMY

THE EFFECT OF ALTEPLASE ON HEALTH CARE UTILISATION AND QUALITY OF LIFE IN SWEDEN, NORWAY AND SCOTLAND: RESULTS FROM THE 3RD INTERNATIONAL STROKE TRIAL (IST-3)

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Background and Aims: Prompt treatment of acute ischaemic stroke with alteplase improves functional outcome. Previous studies of the cost effectiveness of alteplase have used simulated state transition models that have not been validated using within-trial estimates of comparative and cost effectiveness. We aimed to estimate health care utilisation, quality adjusted survival and cost-effectiveness of alteplase in a subset of individual participants in the third International Stroke trial.
Method: IST-3 was an international, multi-centre, randomised open-label trial in patients presenting with acute ischaemic stroke within 6 hours of onset of alteplase + best medical management versus best medical management with blinded assessment of outcome. We obtained linked health care utilisation data on 628 individual participants from Scotland, Norway and Sweden from National electronic health records. Costs were estimated for alteplase therapy and the index and subsequent hospital episodes up to 6 and 18 months post-randomisation. Survival times were adjusted using EQ-5D-3L at baseline, 6 and 18 months to derive quality-adjusted survival times.
Results: Treatment with alteplase reduced health care resource utilization across the 18 month follow-up. The result was driven by a non-trivial reductions in acute hospital inpatient and subsequent day case episodes, which was consistent over the 6 and 18 month follow-up.
Conclusion: We will present the effect of alteplase on quality-adjusted survival and health resource usage in this trial population of older subjects and discuss the generalisability and implications of the results from this unique three-country health economic study.

LB01-004

CLINICAL TRIAL RESULTS – ACUTE MANAGEMENT – THROMBOLYSIS OR THROMBECTOMY

THE ANSTROKE TRIAL

Background and Aims: Retrospective studies have shown worse neurological outcome after endovascular treatment (EVT) for patients with acute ischemic stroke (AIS) managed with general anesthesia (GA) during the procedure, compared to patients managed with conscious sedation (CS). However, all these studies suffer from pronounced selection bias. The AnStroke trial is a single-center, randomized trial, with the aim to compare neurological outcome after EVT in patients randomized to GA or CS.
Method: https://clinicaltrials.gov NCTO1872884
Three-hundred-twenty-one patients were screened for eligibility from Nov 2013 to July 2016 and 106 were subsequently randomized to GA or CS. Ninety patients, 45 in each group, were finally analyzed in relation to mRS 3 months (primary end-point), NIHSS at 24 hours, three days and at discharge or day 4–7. A MRI was performed day three for infarct volume estimation.
Demographics, administration of intravenous thrombolysis, occlusion site, ASPECT score, collateral circulation, blood glucose, blood gas samples and relevant time intervals were recorded. Invasive blood pressure was noted every 5 minutes and anesthesiologists were involved in all procedures. Anesthesiological and interventional complications were recorded.
The choice of embolectomy technique was at the discretion of the neurointerventionist in charge. The angiographic result was defined according to the modified Thrombolysis In Cerebral Ischemia (mTICI) score.
Results: The neurological outcomes, measured as mRS 3 months (primary outcome), NIHSS and infarction volume, for patients randomized to GA or CS before EVT, will be presented at ESOC May 18 2017.
Conclusion: Please see Results section

LB01-005

CLINICAL TRIAL RESULTS – ACUTE MANAGEMENT – THROMBOLYSIS OR THROMBECTOMY

TIME DELAYS AND ENDOVASCULAR TREATMENT EFFECT: A PRESPECIFIED PATIENT-LEVEL POOLED ANALYSIS OF ALL AVAILABLE TRIALS. The VISTA-Endovascular Collaborators

Background and Aims: Time from onset to treatment has been recognized as an important modifier of the effect of endovascular treatment. However, effect estimates have not been precise and the role of other prognostic factors and imaging parameters in conjunction with time has not been addressed sufficiently in previous trial reports and pooled analyses. We pre-specified an individual pooled data (IPD) analysis to test how time from onset modifies the treatment effect of endovascular therapy.
Method: An individual pooled data (IPD) analysis of all eligible trials in the VISTA-Endovascular repository is underway (Int J Stroke 2015;10:136-44). We tested whether predefined time parameters, including time to groin and time to reperfusion modify treatment effect of EVT (with IV rtPA) versus IV rtPA alone. We considered trials with $\geq$85% modern devices and $\geq$20 patients. The primary outcome was the full 90-day modified Rankin Scale at three months (mRS 5–6 combined). We will assess how clinical and imaging parameters affect the relation between time and treatment effect. Sensitivity analyses will expand cohorts to include IV rtPA-ineligible patients, and trials with <85% modern devices and/or <20 patients.
Results: The primary cohort consists of 1683 patients from ESCAPE, EXTEND IA, MR CLEAN, PISTE, REVASCAT, SWIFT PRIME, THERAPY, and THRACE. Preliminary results indicate a strong interaction between treatment effect and time from onset to groin ($p = 0.02$) as well as time from onset to reperfusion ($p = 0.03$).
Conclusion: The effect of endovascular treatment is confirmed to be highly time dependent. Full results will be provided at the presentation.

LB01-006

CLINICAL TRIAL RESULTS – ACUTE MANAGEMENT – THROMBOLYSIS OR THROMBECTOMY

Endovascular revascularization with contact aspiration versus stent retriever in acute Ischemic stroke with large vessel occlusion. The ASTER TRIAL. A Randomized Clinical Trial

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Background and Aims: Benefits of endovascular revascularization with contact aspiration technique versus stent retriever in acute ischemic stroke remains unknown due to lack of evidence from randomized trials. We sought to assess whether thrombectomy with contact aspiration is superior to stent retriever for successful reperfusion among acute stroke patients with large vessel occlusion.
Method: ASTER is a prospective, randomized, controlled, open-label, blinded end-point, clinical trial. Patients with acute ischemic stroke and major occlusion were randomly assigned to frontline contact aspiration group (n = 192) or frontline stent retriever (n = 189) immediately prior mechanical thrombectomy. Primary outcome was the percentage of patients with successful recanalization at the end of angiography.
Results: Between October 2015 and October 2016, a total of 381 patients underwent randomization in 8 comprehensive stroke centers and all were included in intention to treat analysis. The primary efficacy outcome was achieved similarly in aspiration and stent retriever groups (85.4% versus 83.1%; P = 0.53). Similar result was found in sensitivity analysis using mTICI score assessed after frontline strategy alone, or when successful reperfusion was defined as mTICI score 3. Of the clinical efficacy outcomes (early neurological improvement, modified Rankin score at three months), and safety outcomes, we found no significant differences between the two arms.
Conclusion: Among patients with acute ischemic stroke in the anterior circulation undergoing thrombectomy, frontline thrombectomy with contact aspiration vs stent retriever did not result in greater successful reperfusion rate at the end of the procedure. The study findings do not support major differences between contact aspiration and stent retriever frontline reperfusion techniques.
NCT02523261.

LB01-007

CLINICAL TRIAL RESULTS – ACUTE MANAGEMENT – THROMBOLYSIS OR THROMBECTOMY

MODIFIERS OF ENDOVASCULAR TREATMENT EFFECT: A PRESPECIFIED PATIENT-LEVEL POOLED ANALYSIS OF ALL AVAILABLE TRIALS. The VISTA-Endovascular Collaborators

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Background and Aims: The stroke field has progressed, from asking "whether" there is benefit, to "who" will benefit from endovascular therapy (EVT). A post-hoc pooling of five trials with predominantly stent retrievers demonstrated benefit for most patients with anterior circulation occlusions, irrespective of baseline characteristics. We reassess these findings in a broader set of trials using our prespecified analysis plan that includes different definitions of key variables and a novel, sequential approach to incorporating future trials.
Method: An individual pooled data (IPD) analysis of all eligible trials in the VISTA-Endovascular registry is underway (Int J Stroke, 2015). We have tested age (continuous), NIHSS (continuous), and ASPECTS (0–4, 5–7, or 8–10) as treatment effect modifiers of EVT (with IV rtPA) vs. IV rtPA alone on the full, 90-day modified Rankin Scale (mRS; 5–6 combined). We will also test intracranial occlusion location and presence of ipsilateral extracranial carotid occlusion. The primary analysis consists of only trials with ≥85% modern devices and ≥20 patients. Sensitivity analyses will expand the cohorts.
Results: As of 11/MAR/2017, all systematic search-identified, randomized trials testing EVT that were completed worldwide had submitted data to the VISTA-Endovascular trial data repository. The primary cohort consists of 1683 patients from ESCAPE, EXTEND IA, MR CLEAN, PISTE, REVASCAT, SWIFT PRIME, THERAPY, and THRACE trials. Preliminary results of the primary cohort verify EVT treatment effect (adjusted OR 1.94; 95% CI 1.55–2.4) and no interaction by age, NIHSS, and ASPECTS in unadjusted testing.
Conclusion: Endovascular treatment effect remains robust. Full results will be provided at the presentation.

LB01-008

CLINICAL TRIAL RESULTS – ACUTE MANAGEMENT – THROMBOLYSIS OR THROMBECTOMY

THROMBOLYSIS OR ANTICOAGULATION FOR CEREBRAL VENOUS THROMBOSIS (TO-ACT): A RANDOMISED CONTROLLED TRIAL

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Background and Aims: Endovascular treatment (ET) may be beneficial for a subgroup of patients with cerebral venous thrombosis (CVT) who have a high risk of poor outcome, despite anticoagulant treatment. Published experience on ET in patients with CVT is promising, but consists only of non-randomised studies.
Objective: To investigate whether ET improves clinical outcome of patients with CVT.
Method: We performed a multicentre, prospective, randomised, open-label, blinded endpoint (PROBE) trial. Eligible were adults with radiologically proven CVT and one or more risk factors associated with poor outcome: mental status disorder, coma, intracerebral hemorrhage, or thrombosis of the deep venous system. We used web-based randomisation to allocate patients in a 1:1 ratio to ET plus anticoagulation in therapeutic dose (intervention) or anticoagulation alone (control). ET consisted of local intra-sinus application of rt-PA or urokinase, mechanical thrombectomy, or a combination of both. The primary endpoint was the modified Rankin Scale (mRS) score at 12 months. Secondary endpoints included the mRS at 6 months, mortality, and recanalisation at 6 months. Major bleeding complications were the principal safety endpoint. The trial was designed to detect a 20% reduction in poor outcome (mRS 2–6), from 40% to 20%.
Results: Between September 2011 and October 2016, 67 patients were randomised (33 intervention and 34 control) in 14 hospitals in 6

countries. After the first interim analysis in November 2016, the trial was terminated because of futility.
Conclusion: Final results of the TO-ACT trial will be presented at the ESO conference.
Funding: Dutch Heart Foundation.
Trial registration: ClinicalTrials.gov, number NCT01204333.

LB01-009

CLINICAL TRIAL RESULTS – ACUTE MANAGEMENT – THROMBOLYSIS OR THROMBECTOMY

Real-World Applicability of Endovascular Therapy in ICA and/or MCA-M1 Occlusions Treated in the 6–24-hour Window: Subgroup Analysis of the Prospective Trevo Registry

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Background and Aims: The current level-1a evidence for stroke thrombectomy supports a stringent 6-hour time window. The DAWN RCT which assessed the benefit of thrombectomy in strictly-selected patients treated within 6–24-hours was recently stopped after reaching its early efficacy endpoint. We aim to evaluate the safety/efficacy of thrombectomy in a large prospective cohort of late-presenting patients treated outside the more rigid clinical trial setting.
Method: Consecutive Trevo Registry patients fulfilling the basic DAWN trial criteria (ICA and/or MCA-M1 occlusion with pre-morbid mRS0-1) were categorized according to their time-from-last-seen-well to arterial puncture as early ($\leq$6hours) vs. late (6–24hours). Univariate analyses were performed for group comparisons. Multivariate analysis was performed to identify the predictors of good outcomes (pre-specified primary endpoint).
Results: A total of 982 Trevo Registry patients (overall $n = 1846$; period:November/2013-March/2017) qualified for the analysis. As compared to the early-treated patients ($n = 675$), patients treated >6hours ($n = 307$) were slightly younger (median, 67 vs. 69 years, $p = 0.032$), had slightly milder strokes (mean admission-NIHSS, 14.9 ± 6.6 vs. 16.2 ± 5.8, $p = 0.004$), less often received IV t-PA (21.2% vs. 71.5%, $p < 0.0001$), and had higher rates of intracranial-ICA occlusions (29.6% vs. 21.9%, $p = 0.002$), extracranial carotid disease (9.2% vs. 5.2%, $p = 0.024$), right-hemispheric occlusions (53.4% vs. 47.4%, $p = 0.012$) and active smoking (26.6% vs. 18%, $p = 0.003$). Baseline and procedural characteristics were otherwise similar.
Despite significantly longer time to treatment (mean,14.1 ± 22.2 vs. 3.5 ± 1.3; median[IQR], 9.6[7.3–14.4] vs. 3.5 [2.6–4.4], $p < 0.0001$; >12hours:37.3% vs. 0%), late-treated patients had similar rates of reperfusion (mTICI 2b-3,95.4% vs. 93.2%, $p = 0.20$), good outcomes (90-day mRS0-2,59.5% vs. 59.7%, $p = 1.0$), symptomatic intracranial hemorrhage (1% vs. 1.3%, $p = 0.76$), and 90-day-mortality (9.5% vs. 9.9%, $p = 0.90$). Age (OR, 0.975; 95%CI [0.964–0.986]; $p < 0.0001$) and admission-NIHSS (OR, 0.887 [0.862–0.912]; $p < 0.0001$) but not time to treatment (OR, 0.997 [0.985–1.009], $p = 0.62$) were independent predictors of good outcomes.
Conclusion: Our study reinforces the DAWN trial approach and provides favorable generalizability data for thrombectomy within the 6–24-hour window in the "real-world" scenario.

AS02-009

CLINICAL TRIAL RESULTS – ACUTE MANAGEMENT – NEITHER THROMBOLYSIS NOR THROMBECTOMY

A RANDOMISED, PLACEBO-CONTROLLED PHASE 2 TRIAL OF SUBCUTANEOUS INTERLEUKIN-1 RECEPTOR ANTAGONIST IN ACUTE ISCHAEMIC STROKE (SCIL-STROKE)

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Background and Aims: The pro-inflammatory cytokine interleukin-1 (IL-1) has a deleterious role in the pathophysiology of cerebral ischaemia. Administration of IL-1 receptor antagonist (IL-1Ra) markedly attenuates experimental brain injury and is safe and well tolerated. Our objective was to investigate whether subcutaneous (SC) IL-1Ra reduces the peripheral inflammatory response in acute ischaemic stroke.
Method: SCIL-STROKE was a single-centre, double-blind, randomised, placebo-controlled phase 2 study of SC IL-1Ra 100 mg administered twice daily for three days in patients presenting within 5 h of ischaemic stroke onset. Randomisation was stratified for baseline NIHSS score and thrombolysis. Blood sampling for measurement of plasma interleukin-6 (IL-6) and other peripheral inflammatory markers was undertaken at 5 time points. The primary outcome was reduction in concentrations of IL-6 to day 3. Secondary clinical outcomes of survival, length of hospital stay and mRS were recorded at 3 months. Thirty patients per group were required for 80% power at the 5% significance level to detect a difference of 0.75 SD in the primary outcome. We planned to recruit up to 80 patients in total over 30 months to allow for loss to follow-up.
Results: Recruitment has completed with $n = 80$ patients randomised and final 3 month follow-up due in January 2017. This is a placeholder abstract in preparation for presentation of the results of the primary and secondary analyses in a late-breaking clinical trial session.
Conclusion: It is anticipated that this study will inform a definitive phase 3 multi-centre trial of SC IL-1Ra in ischaemic stroke by confirming biological proof-of-concept and providing exploratory clinical outcome data.

LB02-001

CLINICAL TRIAL RESULTS – ACUTE MANAGEMENT – NEITHER THROMBOLYSIS NOR ROMBECTOMY

A RANDOMISED, PLACEBO-CONTROLLED PHASE 2 TRIAL OF SUBCUTANEOUS INTERLEUKIN-1 RECEPTOR ANTAGONIST IN ACUTE ISCHAEMIC STROKE (SCIL-STROKE)

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Background and Aims: The pro-inflammatory cytokine interleukin-1 (IL-1) has a deleterious role in cerebral ischaemia. IL-1 induces peripheral inflammatory mediators, such as interleukin-6 (IL-6), which are associated with worse prognosis after ischaemic stroke. Administration of IL-1 receptor antagonist (IL-1Ra) markedly attenuates experimental brain injury. We therefore investigated whether subcutaneous (SC) IL-1Ra reduces the peripheral inflammatory response in acute ischaemic stroke.
Method: SCIL-STROKE was a single-centre, double-blind, randomised, placebo-controlled phase 2 study of SC IL-1Ra (100 mg administered twice daily for 3 days) in patients presenting within 5 h of ischaemic stroke onset. Randomisation was stratified for baseline NIHSS score (<13, ≥ 13) and thrombolysis. Measurement of plasma IL-6 and other peripheral inflammatory markers was undertaken at five time points. The primary outcome was difference in concentration of natural log (IL-6) as area under the curve (AUC) to Day 3, corrected for baseline pre-randomisation value.
Results: We recruited 80 patients (mean age 72 y, median NIHSS 11.8 [range 4 to 25]) of whom 73% received intravenous thrombolysis. A total of 63 participants ($n = 35$ placebo; $n = 28$ IL-1Ra) had sufficient serial blood samples for the primary analysis. IL-1Ra significantly reduced plasma IL-6 ($p < 0.001$) and similarly reduced plasma C-reactive protein ($p < 0.001$). IL-1Ra was well-tolerated, with no difference in the mean number of doses received between the allocation groups. There were no safety concerns with IL-1Ra in terms of overall serious adverse events or systemic infections.
Conclusion: Our results confirm biological proof-of-concept and inform design of a definitive phase 3 trial of SC IL-1Ra in ischaemic stroke.

LB02-002

CLINICAL TRIAL RESULTS – ACUTE MANAGEMENT – NEITHER THROMBOLYSIS NOR ROMBECTOMY

Feasibility and Safety of Mild Therapeutic Hypothermia in Poor-Grade Subarachnoid Hemorrhage: a Prospective Pilot Study

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Background and Aims: Therapeutic hypothermia (TH) improves the neurological outcome in patients after cardiac arrest and neonatal hypoxic-ischemic brain injury. We studied the safety and feasibility of mild TH in patients with poor-grade subarachnoid hemorrhage (SAH) after clipping or coil embolization.
Method: We enrolled 22 patients with poor-grade SAH (Hunt & Hess Scale 4–5 and modified Fisher Scale 3–4). Patients were allocated randomly to either the TH group (34.5°C) or control group after successful clipping or coil embolization. Eleven patients received TH for 48 h followed by 48 h of slow rewarming. Vasospasm, delayed cerebral ischemia, functional outcome, mortality, and safety profiles were compared between groups.
Results: In the TH group, 10 of 11 (90.9%) patients had a core body temperature of < 36°C for $>95\%$ of the 48-h treatment period. Fewer patients in the TH than control group ($n = 11$ each) had symptomatic vasospasms (18.1% versus 36.4%, respectively) and delayed cerebral ischemia (36.3% versus 45.6%, respectively), but these differences were not statistically significant. At 3 months, 54.5% of the TH group had a good-to-moderate functional outcome (0–3 on the modified Rankin Scale) compared with 9.0% in the control group ($p = 0.08$). Mortality at 1 month was 36.3% in the control group compared with 0.0% in the TH group ($p = 0.09$). Serious adverse events were not significantly different between the groups.
Conclusion: In patients with poor-grade SAH, TH after successful emergency treatment may reduce the risk of vasospasm and delayed cerebral ischemia, improving the functional outcomes and reducing mortality. A larger randomized controlled trial may be warranted.

LB02-003

CLINICAL TRIAL RESULTS – ACUTE MANAGEMENT – NEITHER THROMBOLYSIS NOR ROMBECTOMY

EFFECT OF INTENSIVE VERSUS GUIDELINE ANTIPLATELET THERAPY IN MAJOR ISCHAEMIC STROKE: DATA FROM THE TRIPLE ANTIPLATELETS FOR REDUCING DEPENDENCY IN ISCHAEMIC STROKE (TARDIS) TRIAL

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Background and Aims: The risk of recurrence following an ischaemic stroke (IS) or transient ischaemic attack (TIA) is high, especially immediately after the event. Since one antiplatelet agent is more effective than none, and two are superior to one, more intensive treatment might be even more effective in preventing recurrence providing bleeding does not become a limitation.
Method: TARDIS was an international prospective randomised open-label blinded-endpoint controlled parallel-group trial. Patients with acute non-cardioembolic IS or TIA were randomised to intensive antiplatelet therapy (combined aspirin, clopidogrel and dipyridamole) or guideline antiplatelets (clopidogrel alone, or combined aspirin and dipyridamole) given for 30 days. The primary outcome was recurrent cerebral events and their severity (based on modified Rankin Scale) at 90 days.
Results: 3,096 patients were enrolled from 106 sites in 4 countries between April 2009 and March 2016 (with 71% patients recruited from October 2012). Of these, 884 (29%; Intensive 447, Guideline 437) were enrolled with major stroke (NIHSS > 3). At baseline: mean age 69 (SD 10); male 64%; recruitment from UK 92%; prior stroke 14%; diabetes 21%; onset to randomisation <12 hours 8%, <24 hours 23%.

Conclusion: The results of this analysis will be available for presentation in quarter 2 2016. TARDIS is large enough to influence clinical practice.

LB02-004

CLINICAL TRIAL RESULTS – ACUTE MANAGEMENT – NEITHER THROMBOLYSIS NOR ROMBECTOMY

Effect of intravenous glyburide on adjudicated edema endpoints in the Glyburide Advantage in Malignant Edema and Stroke (GAMES-RP) Trial

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Background and Aims: The GAMES-RP trial tested intravenous (IV) glyburide for the prevention of edema in large hemispheric infarction patients. The primary objective of this analysis was to evaluate the effect of IV glyburide on adjudicated, edema-related endpoints.
Method: GAMES-RP was a prospective, double blind, randomized, placebo controlled phase 2 study that enrolled patients with large hemispheric infarction. Blinded adjudicators assigned designations for edema and edema-related endpoints, including neurological deterioration, malignant edema and edema-related death using *a priori* definitions.
Results: In the per protocol sample, there was no difference in the incidence of malignant edema (46% in IV glyburide; 47% in placebo, $p = 0.94$) or edema-related neurological deterioration (45% IV glyburide; 50% placebo, $p = 0.66$). However, treatment with IV glyburide was associated with a reduced proportion of deaths attributed to cerebral edema (2.4% IV glyburide; 22.2% placebo, $p = 0.01$). Moreover, in patients who experienced malignant edema or edema-related neurological deterioration, there was less midline shift and reduced MMP-9 levels. The rate of NIHSS increase of ≥ 4 during the infusion period (37% IV glyburide; 71% in placebo, $p = 0.043$), and the change in level of alertness (NIHSS subscore 1a; 58% versus 94%; $p = 0.016$] also favored IV glyburide.
Conclusion: IV glyburide was associated with fewer deaths attributed to edema. Interpretation of the rates of malignant edema and neurological deterioration may be confounded by a ceiling effect in severe stroke patients. However, IV glyburide treatment was associated with improvements in midline shift, MMP-9, NIHSS and level of alertness. These data support further study of IV glyburide in a phase 3 trial.

LB02-005

CLINICAL TRIAL RESULTS – ACUTE MANAGEMENT – NEITHER THROMBOLYSIS NOR ROMBECTOMY

Head positioning in high risk patients: post-hoc subgroup analysis of HeadPoST, an international cluster crossover trial

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Background and Aims: The Head Positioning in Stroke Trial (HeadPoST) aimed to determine comparative effectiveness of lying-flat versus sitting-up ($\geq 30^{\circ}$) in patients with acute stroke. The main results were announced and are in press, showing no between-group differences in any disability outcome or serious adverse events (SAEs) including pneumonia. We aimed to explore the effects in further subgroups at potential high risk of harm from lying flat.
Method: HeadPoST was a prospective, cluster crossover, blinded outcome clinical trial involving 11094 patients from 114 hospitals in 9 countries from 2015 to 2016. An average 49 patients were recruited to each head position phase per centre, managed to a usual care policy of positioning applied early and continued for next 24 hours after admission. Treatment effects were assessed in subgroups: reperfusion therapy (thrombolysis/thrombectomy, $n = 1341$), large-artery atheroma ($n = 2948$), intubation/ventilation ($n = 361$), and 3 dysphagia groups - any ($n = 2045$), choked/coughed on eating/drinking ($n = 1560$), and placed on nil-by-mouth regime ($n = 976$).
Results: There was no significant heterogeneity in the treatment effect in patients with large-artery occlusion or who received reperfusion treatment. However, there was an indication that the effects were different for the later two major dysphagia groups for all 3 endpoints: primary disability outcome (ordinal shift in mRS scores), any SAE and pneumonia. The differential effect consistently favoured the lying-flat position.
Conclusion: Secondary analysis of the HeadPoST study suggest differential treatments between lying-flat and sitting-up in patients with dysphagia who are assesses as high risk of aspiration.

LB02-006

CLINICAL TRIAL RESULTS – ACUTE MANAGEMENT – NEITHER THROMBOLYSIS NOR ROMBECTOMY

SAFETY AND EFFICACY OF INTRA-ARTERIAL INFUSION OF BONE MARROW DERIVED MONONUCLEAR CELLS IN SUBACUTE ISCHEMIC STROKE: RANDOMIZED OPEN LABELED CLINICAL TRIAL

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Background and Aims: Stem cells activate and amplify endogenous restorative brain plasticity process. Bone marrow derived mononuclear stem cells (BMSCs) induce changes in serum cytokines and growth factors. Safety, improved outcomes and reductions in lesion volume with stem cells has been observed.

Aim: To assess safety and clinical outcome of intraarterial infusion of bone marrow derived mononuclear cells in subacute ischemic stroke patients

Method: Prospective randomized open label blinded end point assessment was carried out on five cases and ten controls. Subacute ischemic stroke (Day 15–28) with NIHSS 7–15 were randomly assigned to receive intraarterial infusion of autologous BMSCs or standard of care. Primary outcome assessed was safety. Secondary outcomes was efficacy based on modified Rankin scale (mRS 0–2) at day 30, 90 and 180 days.

Results: Patients received mean of $4.16x10^7$ CD 34 positive BMSCs injected in ipsilateral M1 MCA. 231 subjects were screened and 22 randomised Six in BMSC and one control withdrew consent after randomization. Mean age was 61.4 + 12.4yrs, Median NIHSS 12. Median time from onset to cell infusion was 22 days (IQR:15.00 – 39.50),from bone marrow aspiration to infusion-3.20 (IQR 0.4) hours.

No adverse event was observed during infusion and follow up. No difference was observed in outcomes based on mRS (0–2 at 180 days),BI or NIHSS($p = .534$). Two patients died in control arm. No change seen in infarct volume (−3.3 versus −3.37; $P = 0.95$) at day 180. No adverse events observed in two arms

Conclusion: Intra-arterial infusion of BMSCs is safe in subacute ischemic strokes. Study was not powered for clinical efficacy which should be tested in adequately powered study.

LB03-001

CLINICAL TRIAL RESULTS – REHABILITATION & RECOVERY

INTRATHECAL BACLOFEN THERAPY COMPARED TO THE CONVENTIONAL TREATMENT: EFFICACY RESULTS IN THE MANAGEMENT OF POST-STROKE SPASTICITY OF THE SISTERS RANDOMIZED CONTROL TRIAL

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Background and Aims: AS03-019 Intrathecal Baclofen (ITB) is an effective treatment for managing severe spasticity in post-stroke patients. SISTERS, a randomized, controlled, open-label multicenter study compared the efficacy of the ITB therapy versus oral anti-spastic medications (Best Medical Treatment, BMT) in severe spasticity patients.

Method: Sixty stroke patients who presented with spasticity in at least two extremities and an Ashworth Scale (AS) score ≥ 3 in a minimum of two affected muscle groups in the lower limbs were randomized to ITB or BMT arms and evaluated after 6 months of treatment.

Results: At baseline mean (SD) age and time since stroke were 55.89 (9.90) and 4.76 (3.62) years, respectively. After 6 months of treatment the mean AS in the affected lower limbs decreased by 0.99 (0.75) in the ITB group compared to 0.43 (0.72) in the BMT patients ($P < 0.05$). Decrease of AS in upper extremities was 0.66 (0.59) versus 0.17 (0.70) in ITB and BMT groups, respectively ($P < 0.05$). In addition, patients in the ITB arm showed an improvement of 2.68 (10.31) in the Functional Independence Measure. Seven serious adverse drug reactions (SADR, constipation, fecaloma, epilepsy, peripheral edema, hypotension, 2 urinary retention) and 4 serious device reactions (device dislocation, infection, catheter occlusion, intracranial hypotension) were observed in the implanted patients (24% and 16% of patients, respectively) versus 1 SADR (epilepsy) in the BMT group (3%). These serious events were successfully resolved.

Conclusion: This is the first clinical evidence showing superior efficacy of ITB therapy compared to conventional oral medication in decreasing spastic hypertonia in post-stroke patients.

LB03-003

CLINICAL TRIAL RESULTS – REHABILITATION & RECOVERY

CTX HUMAN STEM CELLS IN STROKE RECOVERY: 6 MONTH OUTCOMES OF THE PILOT INVESTIGATION OF STEM CELLS IN STROKE PHASE 2 EFFICACY (PISCES II) STUDY

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Background and Aims: PISCES 2 is an open label single arm study (2012-003482-18) undertaken to determine whether a sufficient proportion of patients with upper limb dysfunction exhibit improvement in arm function following intracranial implantation of *CTX* cell therapy to justify a randomised controlled trial.
Method: Patients with supratentorial ischaemic stroke resulting in upper limb weakness (NIHSS > 1) and functional impairment (Action Research Arm Test [ARAT] sub-test number 2 [grasp] 0–1) were recruited 1 to 10 months post-stroke onset. A single dose of 20 million *CTX* cells was injected by stereotactic surgery into the putamen of the affected hemisphere. Patients were assessed prior to, and at 1, 3, 6, and 12 months post-cell administration.
The primary outcome was a ≥ 2 point improvement in ARAT sub-test 2, at 3 months post-cell administration. Secondary outcomes included changes in ARAT total score, modified Rankin Scale, Barthel Index and Fugl-Meyer scale along with safety and tolerability. Responder analysis for minimal clinically important differences of the secondary outcome measures was undertaken.
Results: Twenty three patients were treated at a median of 7 (IQR 6–11.5) months after stroke onset, 52% male, mean age 65 years (range 41–79). Median NIHSS at enrolment was 7 (IQR 5–8).
Conclusion: Adverse events related to surgery were reported in most patients. No cell-related effects have been evident to date. Six month outcomes will be presented.

LB03-004

CLINICAL TRIAL RESULTS – REHABILITATION & RECOVERY

TALOS: A MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL TO TEST THE VASCULAR AND NEUROPROTECTIVE EFFECTS OF CITALOPRAM IN PATIENTS WITH ACUTE ISCHEMIC STROKE

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Background and Aims: Selective Serotonin Reuptake Inhibitors (SSRI) are effective and safe in the treatment of post-stroke depression (PSD). SSRI may inhibit platelet aggregation and a neuroprotective effect has been suggested. However, data on the efficacy and safety of early SSRI treatment in patients with acute stroke are lacking.
The aim of this trial was to investigate whether early SSRI after ischaemic stroke has 1) a vascular protective effect and 2) an effect on functional ability at 6 months.
Method: A multicenter, randomized, double-blind, placebo-controlled study. We included 641 first-ever ischaemic stroke patients without depressive symptoms within 7 days after onset. Patients were randomized to citalopram or placebo (1:1) as add-on to standard medical care. The two co-primary outcomes were: 1) a composite end-point of vascular death, TIA/recurrent stroke or myocardial infarction and 2) modified Rankin Score (mRS). Secondary effect variables included the individual components of the combined outcome and PSD, and cognitive function.
Data will be analyzed according to the statistical analysis plan described prior to unblinding, including intention-to-treat and per-protocol analyses.
Results: In total, 545 (85%) patients (mean age 68 yrs, 34% female) received treatment for at least 1 month (per-protocol). Patients started treatment in average 2.1 days (SD 1.64) after index stroke. At baseline, NIHSS was 5.0 (SD 5.2) and mRS was comparable in the two treatment arms.
Final results will be presented at the ESOC.
Conclusion: This trial is the largest RCT so far to examine the efficacy and safety of early SSRI treatment after ischemic stroke.

Table (LB03-003)

Results of Responder Analysis	ARAT subtest = 2 point n = 23	ARAT total ≥ 6 point improvement n = 23	mRS ≥ 1 category improvement n = 23	Barthel Index (/100) ≥ 9 point improvement n = 23	Fugl-Meyer ≥ 10 point improvement (motor scale) n = 11
# Responders	3	7	7	8	3

AS04-003

CLINICAL TRIAL RESULTS – PREVENTION

PRASUGREL VERSUS CLOPIDOGREL IN ISCHEMIC STROKE PATIENTS: A MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PARALLEL GROUP TRIAL (THE PRASTRO-I)

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Background and Aims: Prasugrel, a thienopyridine inhibitor of the platelet P2Y12 receptor, has been widely used for patients with acute coronary syndrome. However, the effects of prasugrel for stroke patients have not been clarified.

Method: The PRASTRO-I study was a phase 3, multicenter, randomized, double-blind, parallel group, trial involving 3747 patients (62 ± 9 years old, 797 women) with noncardioembolic ischemic stroke under the age of 75 years and over the body weight of 50 kg from 224 Japanese institutes (JapicCTI-111582). The patients were randomly assigned between 1 and 26 weeks after symptom onset, in a 1:1 ratio, to receive either prasugrel (3.75 mg once daily) or clopidogrel (75 mg once daily) for 96 weeks. The primary objective was to determine whether prasugrel would be noninferior (below a margin of 1.35) to clopidogrel with respect to the primary composite outcome of ischemic stroke, myocardial infarction, or other vascular death.

Results: The primary outcome occurred in 73 of 1885 (3.9%) patients receiving prasugrel, versus 69 of 1862 (3.7%) patients receiving clopidogrel (RR 1.05, 95% CI 0.76–1.44). Any stroke, as a secondary outcome, occurred in 73 patients (3.9%) for both groups (RR 0.99, 95% CI 0.72–1.36). A composite safety outcome of life-threating bleeding, major bleeding, or clinically relevant bleeding occurred in 115 (6.1%) versus 110 patients (5.9%), respectively (RR 1.02, 95% CI 0.79–1.33).

Conclusion: The study did not demonstrate noninferiority of prasugrel over clopidogrel in Japanese patient with noncardioemboric ischemic stroke, though the rates of efficacy and safety outcomes were similar between groups.

AS04-021

CLINICAL TRIAL RESULTS – PREVENTION

THE FURTHER CARDIOVASCULAR OUTCOMES RESEARCH WITH PCSK9 INHIBITOR IN SUBJECTS WITH ELEVATED RISK (FOURIER) TRIAL: EFFECT OF EVOLOCUMAB ON CEREBROVASCULAR DISEASE

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Background and Aims: Low-density lipoprotein cholesterol (LDL-C) is a major risk factor for ischemic cerebrovascular disease. Statins and the combination of statin and ezetimibe have been shown to reduce the risk of non-hemorrhagic stroke as well as other cardiovascular diseases. Evolocumab is a fully human monoclonal antibody inhibitor of proprotein convertase subtilisin/kexin type 9 (PCSK9) that reduces LDL-C by $\approx$ 60%. We tested the hypothesis that evolocumab and optimized statin therapy combined would reduce the incidence of major adverse cardiovascular events including ischemic cerebrovascular events.

Method: FOURIER is a randomized, double blind, placebo-controlled, multinational clinical trial. Patients with a history of myocardial infarction (MI), non-hemorrhagic stroke, or symptomatic peripheral artery disease and either an LDL-C $\geq$ 70 mg/dl or a non-HDL-C $\geq$100 mg/dl on optimized statin therapy were randomized in a 1:1 ratio to evolocumab (either 140 mg SC every 2 weeks or 420 mg SC every month according to patient preference) or matching placebo. The primary endpoint is the composite of cardiovascular death, MI, hospitalization for unstable angina, stroke, or coronary revascularization. The key secondary endpoint is the composite of cardiovascular death, MI, or stroke. Ischemic fatal and non-fatal stroke and TIA is another secondary endpoint.

Results: 27,564 patients were enrolled between February 2013 and June 2015. A total of 19% have a history of non-hemorrhagic stroke. The target of accruing at least 1630 adjudicated key secondary endpoints was achieved late 2016.

Conclusion: Details on the efficacy and safety in patients with a history of non-hemorrhagic stroke and on cerebrovascular outcomes will be ready for presentation.

LB04-001

CLINICAL TRIAL RESULTS – PREVENTION

SPACE-2: STENT-PROTECTED ANGIOPLASTY IN ASYMPTOMATIC CAROTID ARTERY STENOSIS VS. ENDARTERECTOMY COMPARED TO BEST MEDICAL TREATMENT. ONE YEAR RESULTS

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Background and Aims: (ISRCTN 78592017) Recommendations for treatment of asymptomatic carotid artery Stenosis (ACAS) with endarterectomy (CEA) are based on trials recruiting patients more than 15 years ago. Registry data indicate that advances in best medical treatment (BMT) may have led to a decreasing stroke risk in ACAS. The aim of SPACE-2 was to compare the preventive effects of BMT alone, with that of BMT plus CEA or carotid artery stenting (CAS) in patients with ACAS $\geq 70\%^{ECST}$.
Method: 513 patients were randomised to CEA (n = 203), CAS (n = 197) or BMT (n = 113). The primary efficacy end-point (any stroke or death from any cause within 30 days plus ipsilateral ischaemic stroke within 5 years) and further end-points were analysed.
Results: Study was stopped prematurely because of recruitment problems. One-year-rate of the primary endpoint was not significantly different between groups (BMT 0.9%, CEA 2.5%, CAS 3.1%; p = 0.473). Rates of any stroke (BMT 0.9%, CEA 3.9%, CAS 3.6%, p = 0.312). and mortality did not differ significantly between groups (BMT 3.5%, CEA 2.5%, CAS 1.0%; p = 0.304). Higher rates of restenosis occurred in the stenting group (CAS 5.1% vs. CEA 2.0%, p = 0.108).
Conclusion: These interim results from SPACE-2 did not show that CAS or CEA are superior to BMT in primary stroke prevention in patients with a ACAS up to one year after treatment. CAS did not differ significantly from CEA in terms of safety and efficacy in treating ACAS. Follow-up will be performed up to 5 years. Data may be used for pooled analysis with ongoing trials.

LB04-002

CLINICAL TRIAL RESULTS – PREVENTION

CILOSTAZOL VERSUS ASPIRIN FOR A COGNITIVE OUTCOME IN ISCHEMIC STROKE PATIENTS WITH HIGH RISK OF CEREBRAL HEMORRHAGE: PICASSO-COG TRIAL

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Background and Aims: Multiple cerebral microbleeds (CMBs) and prior intracerebral hemorrhage (ICH) are associated with higher risk of cognitive decline after stroke. We aimed to investigate the differences of cilostazol and aspirin to prevent cognitive decline in stroke patients with multiple CMBs or prior ICH.
Method: PreventIon of CArdiovascular events in iSchemic Stroke patients with high risk of cerebral hemOrrhage for reducing COGnitive decline (PICASSO-COG) is a randomized controlled trial with 61 institutes from South Korea. Patients with noncardioembolic ischemic stroke within 180 days with previous ICH or multiple CMBs were randomized to cilostazol versus aspirin groups. Mini-mental state examination (MMSE) was conducted at 4 (baseline), 13, 25, 37, and 49 months after index-stroke. Primary outcome was the change in MMSE score over time from baseline, which was analyzed using mixed effects model.
Results: A total 892 subjects were included in the analysis, with a median follow-up of 20.9 months. Mean changes of MMSE from baseline to each follow-up was 0.02 ± 2.45 (1^{st}, n = 888), -0.15 ± 2.65 (2^{nd}, n = 593), -0.24 ± 3.11 (3^{rd}, n = 361), and -0.88 ± 3.06 (4^{th}, n = 138). Changes in MMSE scores over time did not differ between treatment groups (Figure). Subgroup and sensitivity analyses also showed negative results.
Conclusion: There were no significant differences with cilostazol and aspirin to prevent cognitive decline after stroke in patients with high risk of cerebral hemorrhage.

AS06-048

SYSTEMATIC REVIEW AND META-ANALYSIS

RESUMPTION OF ORAL ANTICOAGULATION AFTER INTRACEREBRAL HEMORRHAGE IS ASSOCIATED WITH DECREASED MORTALITY AND FAVORABLE FUNCTIONAL OUTCOME

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Background and Aims: Oral-Anticoagulation-Treatment (OAT) resumption is a dilemma in Intracerebral Hemorrhage (ICH) care, particularly for lobar hemorrhages related to Cerebral-Amyloid-Angiopathy. We sought to determine whether OAT resumption after ICH is associated with decreased mortality and favorable long-term outcome, accounting for ICH location (i.e. lobar vs. non-lobar).
Method: We meta-analyzed individual-patient-data from: 1) the multicenter-RETRACE study conducted in Germany (n = 542); 2) a longitudinal ICH study conducted in Boston (n = 268); 3) the Ethnic/Racial-Variations-of-Intracerebral-Hemorrhage (ERICH) study (n = 217). We determined whether, at one year from ICH, OAT resumption was associated with: 1) mortality; 2) favorable functional outcome (mRS:0–3); stroke incidence. We separately analyzed non-lobar and lobar ICH cases using propensity score matching and multivariable (Cox regression) models.
Results: We included 1027 survivors of OAT-related ICH (641 non-lobar and 386 lobar). Among non-lobar ICH survivors 179/641(28%) resumed OAT, while 88/386(23%) lobar ICH survivors did. In multivariable analyses OAT resumption after non-lobar ICH was associated with decreased mortality (HR = 0.22, 95%CI = 0.16–0.30, $p < 0.0001$) and improved functional outcome (HR = 5.12, 95%CI = 3.86–6.80, $p < 0.0001$) at one year. OAT resumption after lobar ICH was also associated with decreased mortality (HR = 0.25, 95%CI = 0.17–0.38, $p < 0.0001$) and favorable functional outcome (HR = 4.89, 95%CI = 3.25–7.36, $p < 0.0001$). Furthermore, OAT resumption was associated with decreased all-cause stroke incidence in both lobar ICH (HR = 0.51, 95%CI = 0.32–0.80, p = 0.004) and non-lobar ICH (HR = 0.45, 95%CI = 0.28–0.71, p = 0.0008).
Conclusion: We provide novel evidence of association between OAT resumption, decreased mortality, and favorable outcome following ICH, regardless of hematoma location. We also identified an association between OAT resumption and decreased stroke incidence after both non-lobar and lobar ICH. These findings support conducting randomized clinical trials to explore risks and benefits of OAT resumption after ICH.

AS06-016

SYSTEMATIC REVIEW AND META-ANALYSIS

LONG-TERM ANTITHROMBOTIC TREATMENT IN INTRACRANIAL HEMORRHAGE SURVIVORS WITH ATRIAL FIBRILLATION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background and Aims: The risk-benefit ratio of antithrombotic therapies for stroke prevention in intracranial haemorrhage (ICH) survivors with atrial fibrillation (AF) remains unknown. We performed a systematic review and meta-analysis of studies reporting recurrent ICH and ischemic stroke (IS) in ICH survivors with AF during long-term follow-up.
Method: A comprehensive literature search including MEDLINE, EMBASE, Cochrane library, clinical trials registry was performed following the PRISMA statement. We considered studies capturing outcome events (ICH recurrence and IS) for ≥3 months and treatment exposure to vitamin K antagonists (VKA), antiplatelet agents (APA) or no antithrombotic medication (no-ATM). Corresponding authors provided aggregate data for IS and ICH recurrence rate between 6 weeks after the event and 1 year of follow-up for each treatment exposure. Meta-analyses of pooled rate ratios (RR) were conducted using the inverse variance method.
Results: 17 articles met inclusion criteria. Seven observational studies enrolling 2452 patients were included in the meta-analysis. Pooled RR estimates for IS were lower for VKA compared to APA (RR = 0.45, 95% CI: 0.27–0.74, p = 0.002) and no-ATM (RR = 0.47, 95% CI: 0.29–0.77, p = 0.002). Pooled RR estimates for ICH recurrence were not significantly increased across treatment groups (VKA vs APA RR = 1.34; 95% CI: 0.79 to 2.30, p = 0.28; VKA vs no-ATM RR = 0.93, 95% CI: 0.45 to 1.90, p = 0.84).
Conclusion: In observational studies, anticoagulation with VKA is associated with a lower rate of IS than APA or no-ATM without increasing ICH recurrence substantially. A randomized controlled trial is needed to determine the net clinical benefit of anticoagulation in ICH survivors with AF.

AS08-004

THROMBOLYSIS – EXCLUDING CLINICAL TRIAL RESULTS

MILD STROKE DUE TO LARGE ARTERY OCCLUSION. WHEN IS IV THROMBOLYSIS NOT ENOUGH? RESULTS FROM THE SITS-ISTR REGISTRY

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Background and Aims: We aimed to determine the frequency, risk factors and 3 month outcomes of non-hemorrhagic early neurological deterioration (nhEND) in patients suffering IVT-treated minor stroke, with versus without associated occlusion of large proximal and distal cerebral arteries.
Method: We analysed data from the SITS-International Stroke Thrombolysis Register on 2553 patients with IVT-treated minor stroke (NIH Stroke Scale (NIHSS) scores 0–5) and available arterial occlusion data. nhEND was defined as an increase in NIHSS score ≥ 4 at 24 hours, without parenchymal hematoma on follow-up imaging within 22–36 hours. Adjusted OR were determined for groups with LAO compared to those with no occlusion.
Results: Frequency of nhEND diminished from 30% of patients with terminal internal carotid (ICA-T) or tandem occlusions (ICA + middle cerebral artery (MCA) (adjusted OR: 10.3, $p < 0.001$), through 17% in extracranial carotid occlusions (aOR 4.3, $p < 0.001$) and 9% (aOR 2.1, $p = 0.06$) with proximal MCA-M1 occlusion, to only 3.1% in those without occlusion. Death or dependency (mRS 3–6) at 3 months occurred in 77% (95% CI 60.2–88.6%) of patients with any occlusion and nhEND, in 10.9% (8.2–14.5%) in occlusion without nhEND and in 10.8% (9.2–12.6%) of patients without occlusion.
Conclusion: Patients with apparently minor stroke associated with occlusion of the ICA, with or without tandem MCA involvement, are at high risk of disabling deterioration, despite IVT treatment. Acute vessel imaging is desirable even in minor stroke patients to identify and consider endovascular treatment for those who may be at high risk of preventable deterioration.

LB18-001

ATRIAL FIBRILLATION, CARDIOEMBOLISM & HEART-BRAIN INTERACTIONS

Early Prolonged Ambulatory Cardiac Monitoring in Stroke (EPACS): Randomised Clinical Trial using patch-based cardiac monitoring

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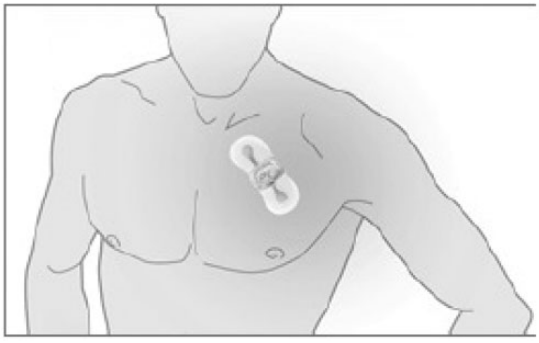
Background and Aims: Cardioembolism in paroxysmal atrial fibrillation (PAF) is a preventable cause of ischaemic stroke or transient ischaemic attack (TIA), but the transient nature of PAF means that a short-duration Holter monitor misses a significant proportion of cases. Systems for recording beyond 3–7 days have significant limitations: event-triggered loop recorders are cumbersome while implanted loop recorders require a minor surgical procedure. There is a need for patient-friendly long-duration cardiac monitoring systems for stroke patients.
Method: Pragmatic randomised controlled trial of cardiac monitoring after an ischaemic stroke or TIA (recruited <3 days of index event) randomised 1:1 to use either a wearable water-proof adhesive cardiac monitoring patch (Zio® Patch, iRhythm Technologies Inc) fitted immediately by the clinician early after the index event or a standard Holter ECG. ISCRTN Registration 50253271. The total patients recruited was 120 patients across two hospital sites with large stroke units:
- Kings College Hospital, London (urban teaching hospital)
- Princess Royal University Hospital (suburban district hospital)



Results: The interim analysis of the first 87 patients should more PAF in the active arm which had not yet reached statistical significance in January 2017. Those in the control arm of Holter ECG's had significant delays to initiate cardiac monitoring due to scheduling delays and patient non-attendance. There were no device-attributable serious adverse events. Late-breaking results with the full target study population will be presented.
Conclusion: The convenience of the patch-based cardiac monitor substantially increased the uptake and efficiency of cardiac monitoring early after ischaemic strokes and TIA, and may have superior PAF detection rate to standard approaches.

AS21-056

IMAGING – HYPERACUTE

COMPARING THE IMPACT OF BASELINE COLLATERAL STATUS ASSESSED BY DIFFERENT COLLATERAL SCORES AND IMAGING MODALITIES ON OUTCOMES IN ACUTE ISCHEMIC PATIENTS: META-ANALYSIS FROM THE HERMES-COLLABORATION

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Background and Aims: Good leptomeningeal collaterals are associated with smaller infarct volumes, higher rates of recanalization and improved functional outcome after acute stroke treatment (Endovascular therapy [EVT] and/or intravenous tPA [IVT]). However, assessment of collateral status on acute imaging is not standardized and the impact of imaging type and scan quality on collateral grading is poorly understood. The aim of this study is to compare different CTA/MRA based collateral scores and imaging modalities.
Method: Patients from the HERMES collaboration (Highly Effective Reperfusion evaluated in the Multiple Endovascular Stroke Trials) will be included in this pre-specified pooled meta-analysis. Collateral status will be assessed on single and multi-phase CTA and on MRA (TOF or CE) using the following collateral scoring systems: TAN Score, modified TAN Score, Regional Collateral Score for (i) single phase and (ii) multiphase CTA and the Regional Leptomeningeal (ASPECTS) Score. Scan quality will be assessed using multiple parameters including timing of acquisition, coverage, motion artifacts etc. Collateral scores and imaging modalities will be compared to each other in discrimination of imaging (infarct volumes and ASPECTS on follow-up scans) and clinical (dichotomized modified Rankin Scale [mRS) and mRS shift at 90 days) outcomes using Receiver operating curve analysis (ROC), Akaike information criterion (AIC) and Bayesian information criterion (BIC). Sensitivity analyses correcting for acquisition phase will be attempted. Imaging analysis is complete and final results will be presented.
Results: Placeholder abstract
Conclusion: Placeholder abstract
A complete author's list will be send by mail.

LB30-001

ONGOING TRIALS

DIAGNOSIS OF COGNITIVE FUNCTIONS: PROBLEMS AND PROSPECTS

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Background and Aims: to study pre-clinical abnormalities of visualspatial gnosis using computer method of 3D rotating object recognition.
Method: 90 subjects. Group I – young people with normal cognitive status. Group II – healthy middle-aged people. Group III – patients after stroke with mild cognitive impairment. ***Cognitive function condition was assessed*** using the mini-mental state examination (MMSE), frontal assessment battery (FAB) and the clock drawing test (CDT), The Montreal cognitive assessment (MoCA), neuropsychological testing by A. R. Luria. Visuospatial and object perception was assessed using a new, specially designed computer assessment tool of three-dimensional recognition of rotating objects. Diagnostic criteria include the speed of the object recognition in different projections and an angle of the object location in the axes X, Y, Z in the moment of recognition recorded by the software.
Results: Slower speed of recognizing both two- and three-dimensional objects was revealed in Group II and Group III. When presented with three-dimensional objects, healthy middle-aged people demonstrated later recognition, with the value of the angle of view 20–30% larger than Group I. The qualitative and quantitative assessment of the cognitive functions I and II groups of subjects characterized by the norm/ When presented with three-dimensional objects, patients after stroke demonstrated later recognition, with the value of the angle of view 49% (axis X), 41% (axis Y) and 36% (axis Z) larger than Group II.
Conclusion: Diagnostic criteria of this new method correlate with clinical manifestations in post-stroke patients, as well as show the early signs of visuospatial impairment in healthy subjects.

LB30-002

ONGOING TRIALS

The dynamics of intracranial, mean arterial and cerebral perfusion pressure by changing the position of the head patients with subarachnoid hemorrhages

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Background and Aims: There is not defined the optimal position of the head in patients with subarachnoid hemorrhage (SAH). We stadied dynamics of intracranial (ICP), cerebral perfusion (CPP) and mean arterial pressure (MAP) by changing the position of the head at patients with SAH.
Method: 74 patients with SAH were studied. Multimodal monitoring includes ICP, MAP and CPP measurement. At the beginning baseline values were obtained in a position 30°, then was lowered by horizontal position (0°), after that elevated by 60°, and at the end was lowered to 30°.
Results: ICP in the horizontal position were 33% higher, than at 30 and 60° in the first day. Minimal values of CPP were registered at 30°. In 60° CPP was on 5,5% higher, than at 30° and reached 91 (81,5–99) mm Hg. Also in 0° at patients with SAH by 5% increased MAP. In second day maximal ICP and critically low CPP were registered in 0°. In 60° ICP was elevated for 3% and CPP decreased by 5,5% in 30°. MAP were maximal in the horizontal position. On third day the difference of values between 30° and 60° disappeared. For the fifth days ICP increase in 0°.
Conclusion: The optimum position of the first day should be considered 60°, since in this position does not increase ICP. On the second day the most favorable angle becomes 30°. By the third day of the difference metrics at position 30° and 60° disappear. On the fifth day again become a preferred 30°.

LB30-003

ONGOING TRIALS

The hospital transportation of patients with subarachnoid hemorrage

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Background and Aims: Transportation of patients with acute cerebral pathology has its own characteristics and principles. Our aim was to optimize transportation of patients with subarachnoid hemorrhages (SAH).
Method: 60 patients with SAH (mean age - 50,39 ± 8,7 years) were studied. Cerebral blood flow (CBF) velocity in middle cerebral artery (MCA) and Lindegaard's index (LI) was estimated to five minutes before transportation and immediately after it through transcranial Doppler. Patients were divided into two groups: 50 patients were transported by the standard clinic practice. 10 patients transported using mechanical ventilation with intravenous nimodipine (1 mg / hr).
Results: In first group CBF in MCA on the operated hemisphere increased by 23.5% (from 131 (118–158) to 149 (135–170) cm / s). On the intact hemisphere CBF increase by 12% (from 120 (110–143) to 130 (117–150) cm / s). LI increase insignificantly. In second group CBF in MCA on the operated hemisphere increased by 4,5%: from 150,5 (136–177) to 153,5 (140–179) cm / s. On the intact hemisphere CBF in MCA increased by 6,2%: from 125 (115–135) to 130 (120–134) cm / s. LI decreased as the operated hemisphere (from 2,9 (2,6–3,0) to 2,7 (2,5–2,8)) and on the intact hemisphere (from 2,3 (1,8–2,7) to 2,1 (1.8–2.4)).
Conclusion: 1. During standard transportation was a significant increase CBF in MCA (23.5%) on the operated hemisphere.
2. Continuous intravenous administration of nimodipine and additional sedation in patients on mechanical ventilation can reduce the CBF increase to 4.5%.
3. Cerebral vasospasm may be regarded as an undesirable effect of transportation.

LB30-004

ONGOING TRIALS

PRECIOUS: PREvention of Complications to Improve OUtcome in elderly patients with acute Stroke. A randomised, open, phase III, clinical trial with blinded outcome assessment

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Background and Aims: PRECIOUS: ISRCTN82217627 - Ongoing Trial Elderly patients are at high risk of complications after stroke, such as infections and fever. These complications are strongly and independently associated with a higher risk of death or dependency. PRECIOUS will assess whether prevention of aspiration, infections, and fever with metoclopramide, ceftriaxone, paracetamol, or any combination of these in the first 4 days after stroke onset improves functional outcome at 90 days in elderly patients with acute stroke.
Method: International, multi-centre, multi-factorial, randomised, controlled, open-label clinical trial with blinded outcome assessment in 3800 patients aged 66 years or older with acute ischaemic stroke or intracerebral haemorrhage and an NIHSS score ≥ 6. Patients will be randomly allocated in a 2*2*2 factorial design to any combination of open-label oral, rectal, or intravenous metoclopramide (10 mg thrice daily), intravenous ceftriaxone (2000 mg once daily), oral, rectal, or intravenous paracetamol (1000 mg four times daily), or usual care, started within 12 hours after symptom onset and continued for 4 days or until complete recovery or discharge from hospital, if earlier. Investigators will have the opportunity to censor a single specific stratum in a specific patient before randomisation. The primary outcome measure is the score on the modified Rankin Scale at 90 days (± 14 days), as analysed with multiple regression.
Results: Planning: First patient included May 2016; final follow-up of the last patient by April 2020
Conclusion: Information: www.precious-trial.eu
Funding: PRECIOUS is funded by the European Union's Horizon 2020 Research and Innovation Programme under grant agreement No 634809.

LB30-005

ONGOING TRIALS

THE T3 TRIAL: TRIAGE, TREATMENT AND TRANSFER OF PATIENTS WITH STROKE IN EMERGENCY DEPARTMENTS

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[9]Ottawa Health Research Institute, Clinical Epidemiology Program, Ontario, Canada
[10]Monash University, Department of Medicine, Clayton, Australia
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[19]University of Ottawa, School of Epidemiology- Public Health and Preventive Medicine, Ontario, Canada
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Background and Aims: Placeholder abstract number: AS01-007]. The T^3 cluster randomised trial aimed to improve **T**riage, **T**reatment and **T**ransfer (T^3) of patients with acute stroke in emergency departments (EDs)
Method: Our prospective, multicentre, parallel group, cluster randomised trial with blinded outcome assessment, randomised EDs 1:1 to receive either the T^3 intervention or no support (control EDs). Our evidence-based intervention targeted: (1) **T**riage: patients with suspected stroke assigned to Australian Triage Scale category 1 or 2 (seen within 10 minutes); (2) **T**reatment: screening for tPA eligibility and administration of tPA where applicable; protocols for management of fever, hyperglycaemia and swallowing; and (3) rapid **T**ransfer from ED to the stroke unit, implemented using (i) workshops to determine barriers and solutions; (ii) education; (iii) use of clinical opinion leaders; (iv) email, telephone and site visit reminders. Primary outcome: 90-days post-admission death or dependency (mRS > 2). Secondary outcomes: 90-day: health status (SF-36), functional dependency (Barthel Index), quality of life (EQ-5D); and in-hospital quality-of-care outcomes: triage practices; monitoring and management for thrombolysis, fever, hyperglycaemia, swallowing; and transfer practices.
Results: Of the 26 eligible sites from three states and one territory in Australia, all (100%) agreed to participate with 2253 patients consenting (pre-implementation n = 645; post-implementation n = 1608). Of these, 1875 will be analysed (pre-implementation n = 574; post-implementation n = 1301). In the post-implementation cohort, 749 patients were randomised to the intervention group and 552 to the control group. Data currently are being analysed.
Conclusion: This large trial will provide rigorous evidence for assisted implementation of nurse-initiated ED stroke protocols aiming to improve outcomes for patients with stroke.

LB30-006

ONGOING TRIALS

MR CLEAN-NO IV: INTRAVENOUS TREATMENT FOLLOWED BY INTRAARTERIAL TREATMENT VERSUS DIRECT INTRAARTERIAL TREATMENT FOR ACUTE ISCHEMIC STROKE CAUSED BY A PROXIMAL INTRACRANIAL OCCLUSION

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Background and Aims: Several trials have shown that intra-arterial treatment (IAT) following intravenous alteplase (IVT) improves outcome of patients with acute ischemic stroke and a proximal intracranial occlusion. However, small subgroups of included patients had contraindications for IVT. Treatment effect of IAT in these patients was at least as effective as in patients treated with IVT prior to IAT. The question arises whether IVT is beneficial in patients eligible for IAT.
Method: The MR CLEAN-NO IV trial is a multicenter, prospective, randomized, open-label, blinded-endpoint trial, comparing IVT followed by IAT with direct IAT in patients with a confirmed occlusion of the intracranial carotid artery, M1 or proximal M2. The aim is to include 540 patients. The primary endpoint is the modified Rankin Scale score (mRs) at 90 days. Secondary endpoints include eTICI score, mortality and Barthel score at 90 days. Safety endpoints include sICH and embolization in a new territory on angiography during IAT.
The primary effect parameter is the common odds ratio of the mRs, estimated by ordinal logistic regression. We will adjust for age, pre-stroke mRs, time from onset to randomization, stroke severity and collateral score. Both superiority and non-inferiority are assessed. Secondary outcomes will be analyzed using linear, logistic or ordinal regression analyses as appropriate.
Results: Expected enrollment 1st patient July 2017.
Conclusion: We hypothesize that direct IAT may lead to an 8% absolute increase in good outcome due to a reduction in the occurrence of sICH and an increase in the treatment effect of IAT.

LB30-007

ONGOING TRIALS

PROSPECTIVE REGISTRY OF DECOMPRESSIVE SURGERY FOR CVT PATIENTS – DECOMPRESS – 2

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Background and Aims: Background: several retrospective registries showed that decompressive surgery is lifesaving in patients with acute severe cerebral venous thrombosis (CVT) and parenchymal lesions with impeding herniation. However, retrospective design and publication bias may overestimate the effect of the intervention. Objective: to describe in a prospective registry the vital and functional outcome of CVT patients treated by decompressive surgery, and to identify subgroups of CVT patients who benefit most from this surgery.
Method: Inclusion criteria: consecutive cases of CVT with parenchymal lesions treated by decompressive craniectomy or hematoma evacuation. Outcomes measured at 6 and 12 months by an investigator not directly involved in the surgical intervention. The opinion of the patient and main caregiver concerning the results of surgery is registered. Evaluation of cognition, mood, anxiety, Quality of life, caregiver burden and professional life is performed at 6 and 12 months follow up using MMSE, HADS, EuroQol, Expanded Caregiver Strain Index and Post Stroke working Activity Questionnaires.
Results: Sample size: we aim to collect 100 patients with the contribution of 80 recruiting centres. Primary outcome and prognostic variables: the primary outcome is the modified Rankin Scale dichotomised between favourable (0–4) and unfavourable outcome (5 or death) at last available follow up. Prognostic variables are age, delay to surgery, Glasgow Coma Scale score, fixed pupils, lesion characteristics, and type of surgery.
Conclusion: Current status: inclusion started in January 2012. By 30th March 2017, 66 centres (12 recruited) are currently participating in the study and 54 patients are already included.

LB30-008

ONGOING TRIALS

Solitaire™ With the Intention For Thrombectomy Plus Intravenous t-PA Versus DIRECT Solitaire™ Stent-retriever Thrombectomy in Acute Anterior Circulation Stroke (SWIFT DIRECT)

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Background and Aims: Whether pre-treatment with intravenous thrombolysis (IVT) prior to mechanical thrombectomy (MT) with stent retrievers is beneficial has become a matter of debate. In a patient-level pooled analysis of five randomized controlled studies (HERMES collaboration) similar rates of functional independence and mortality at 90 days were observed between patients who received IVT + MT or MT alone. SWIFT DIRECT aims to determine, whether direct MT in patients with proximal vessel occlusion in the anterior circulation is non-inferior to IVT + MT.
Method: The international, multicentre, randomised-controlled, two-arm, open label, blinded endpoint (PROBE) trial SWIFT DIRECT will randomise 404 patients into the experimental arm (direct MT; 202) or control arm (bridging thrombolysis; 202). The trial will only be performed in patients with immediate access to MT. Main inclusion criteria are signed informed consent, age >18 and <86 years, confirmed ischaemic stroke, NIHSS ≥ 8 and <30 and eligibility for IVT and MT. The primary outcome is functional independence (mRS) ≤ 2 at 90 days. Main secondary outcomes are: mortality, change in NIHSS score post randomization, time to reperfusion (TICI $\geq$ 2b) and quality of life.
Results: We will start recruitment in August 2017 with overall approximately 30 sites in Switzerland, Germany, Austria, France, Spain, Portugal and Canada.
Conclusion: If direct MT in patients with large artery vessel occlusion in the anterior circulation is as safe and efficacious as IVT + MT this would have a relevant impact on future stroke management. Maintaining a high recruitment rate will be crucial for the successful completion of the trial.

LB30-009

ONGOING TRIALS

EARLY VERSUS LATE INITIATION OF DIRECT ORAL ANTICOAGULATION IN POST-ISCHAEMIC STROKE PATIENTS WITH ATRIAL FIBRILLATION (ELAN)

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Background and Aims: When to start anticoagulation in patients with an acute ischaemic stroke and atrial fibrillation (AF) is a relevant unanswered question in clinical practice. Direct oral anticoagulants (DOACs) are highly effective for secondary stroke prevention in these patients, but DOACs were never initiated <7 days after stroke onset in recent trials. The ELAN trial will determine the net benefit of early versus late initiation of DOACs in patients with acute ischaemic stroke related to AF.
Method: The international, multicentre, randomised-controlled, two-arm, assessor-blinded trial ELAN will randomise 2'000 patients into the experimental arm (early treatment; 1'000) or control arm (late treatment, 1'000). T DOACs initiation will vary depending on stroke size. Main inclusion criteria are signed informed consent, age >18 years, confirmed ischaemic stroke and AF and agreement of treating physician to prescribe DOACs. The primary outcome is a composite of major bleeding, recurrent ischaemic stroke, systemic embolism and/or vascular death at 30 ± 7 days after randomisation.
Results: We will start recruitment in July 2017 with currently approximately 80 sites in Switzerland and 7 other European countries.
Conclusion: This pragmatic investigator-initiated international trial will add evidence to the best time of starting DOAC after ischaemic stroke in patients with AF. If earlier initiation of DOACs in patients with ischaemic stroke related to AF is shown to be safe and efficacious, this could have a major impact on better treatment adherence, length of hospital stay and patient outcome.

LB30-010

ONGOING TRIALS

MR CLEAN MED – THE EFFECT OF PERIPROCEDURAL MEDICATION IN PATIENTS UNDERGOING INTRA-ARTERIAL TREATMENT FOR ACUTE ISCHEMIC STROKE: HEPARIN, ANTIPLATELET AGENTS, BOTH OR NEITHER

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Background and Aims: Rapid intra-arterial treatment in patients with acute ischemic stroke with confirmed proximal intracranial occlusion has been proven safe and effective. Still, many patients do not recover despite recanalization. Yet, it is unknown whether periprocedural anticoagulant medication in patients with acute ischemic stroke treated with intra-arterial treatment can improve clinical outcome. The objective of this study is to assess the effect of acetylsalicylic acid and unfractionated heparin, alone, or in combination, in patients with acute ischemic stroke who undergo intra-arterial treatment.
Method: MR CLEAN MED is a multicenter, prospective, randomized, open-label, blinded-endpoint trial using a 2x3 factorial design. We planned to enroll 1,500 patients with a clinical diagnosis of acute ischemic stroke and confirmed intracranial anterior circulation occlusion, who will undergo intra-arterial treatment with or without prior intravenous thrombolysis according to standard care. Study interventions: intravenous treatment with moderate dose unfractionated heparin (loading dose of 5000 IU followed by 1,250 IU/hour x 6 hours), low dose unfractionated heparin (loading dose of 5000 IU followed by 500 IU/hour x 6 hours) and acetylsalicylic acid (300 mg). Primary outcome is the score on the modified Rankin Scale 90 days after inclusion in the study. Safety endpoints include the occurrence of symptomatic intracerebral hemorrhage.
Results: Expected enrollment of 1st patient: July 2017.
Conclusion: We hypothesize that despite the potentially increased risk of (symptomatic) intracerebral hemorrhage, periprocedural unfractionated heparin and/or acetylsalicylic acid will improve functional outcome of patients with acute ischemic stroke treated with intra-arterial treatment.
Sponsored by the Dutch Heart Foundation.

LB30-011

ONGOING TRIALS

Multicenter Randomized Clinical Trial of Endovascular Stroke treatment in The Netherlands for Late arrivals: MR CLEAN-LATE

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Background and Aims: Intra-arterial treatment (IAT) for acute ischemic stroke caused by an anterior circulation proximal intracranial occlusion, in whom the procedure can be started within 6 hours from onset, has been proven safe and effective. Currently there is no proven effective recanalization therapy beyond this 6 hour tme window. We hypothesize that IAT is effective for patients treated between 6 and 12 hours after symptom onset or last seen well less than 12 hours, after selection based on collateral flow.
Method: The MR CLEAN-LATE trial is a multicenter, prospective, randomized, open-label, blinded-endpoint trial, comparing IAT with no IAT between 6 and 12 hours after symptom onset, in acute anterior circulation ischemic stroke caused by a proximal intracranial anterior circulation occlusion (distal intracranial carotid artery or middle (M1/M2) or anterior (A1/A2) cerebral artery confirmed by neuro-imaging (CTA or MRA)). Only patients with poor, moderate, or good collateral flow will be included. The aim is to include 500 patients. Inclusion of poor collateral status will be restricted to 100 patients. The primary endpoint is the modified Rankin Scale score (mRs) at 90 days. Secondary outcomes include mortality at 90 days, hemorrhage and stroke severity at 24 hours and 5–7 days, recanalization on CTA at 24 hours and infarct size on NCCT at 5–7 days or just before discharge.
Results: Expected enrollment of the 1st patient: July 2017.

Conclusion: We expect to demonstrate a treatment effect with a shift on the mRS leading to at least an 8% difference in good outcome in favor of IAT.

LB30-012

ONGOING TRIALS

The benefit of EXtending oral antiCOAgulant treatment after acute Cerebral Vein Thrombosis (EXCOA-CVT): a cluster observational study

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Background and Aims: After cerebral vein thrombosis (CVT) there is an increased risk of further venous thromboembolic events (VTEs). Guidelines suggest oral anticoagulation (OAC) for 3 to 12 months after a first episode of CVT, depending on event-related features and thrombophilic characteristics. Recommendations are extrapolated from extracerebral vein thrombosis, which may be inaccurate as the risk of thrombotic recurrence is different.
EXCOA-CVT is a prospective study with a cluster-randomised allocation design that aims to compare a policy of standard (3–6 months) versus extended (12 months) OAC in the prevention of VTEs after CVT.
Method: Participating centres are asked whether they have preference for any of the policy treatment options. Centres with no preference are randomly allocated for one of the two options. Adult subjects with confirmed CVT are treated according to the approach allocated to their centre as soon as their acute clinical situation is stable and not more than 1 month after CVT diagnosis. Those with conditions judged by the investigator to be absolute indication for prolonged OAC are excluded. Follow-up is performed at 6, 12, 18 (telephone-interview) and 24 months. Primary efficacy outcome is any symptomatic and confirmed VTE (recurrent CVT or other systemic VTE) or death associated with venous thromboembolism. Primary safety endpoints include bleeding events (major/minor and according to the site), and death from any cause.
Results: At present, a total of 386 subjects with CVT have been included from 29 active centres.
Conclusion: The results of this study will provide crucial evidence regarding optimal duration of OAC after CVT.

LB30-013

3ONGOING TRIALS

POSTURAL STABILITY IN PATIENT AFTER ISCHEMIC STROKE

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Background and Aims: The aim of the study is to compare postural stability between ischemic stroke patients and control group.
Method: A total of 13 ischemic stroke patients and 15 age-matched patients without stroke incident as control group were recruited in this study. All patients were evaluated by the Postural Stability test on stability platform.
Results: There were a significant difference in Global Stability Index (%) in stroke patients compared to control group.
Conclusion: There were significantly worse in parameters of PS test in stroke patients group.

LB33-001

WOMEN AND STROKE

DAWN in full daylight (DWI or CTP Assessment with Clinical Mismatch in the Triage of Wake Up and Late Presenting Strokes Undergoing Neurointervention)

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Background: The efficacy of mechanical thrombectomy for acute stroke due to large vessel occlusion (LVO) initiated beyond 6 hours of time last seen well (TLSW) has not been demonstrated by randomized trials.
Aim: To establish whether subjects considered to have substantial areas of salvageable brain based on age-adjusted clinical core mismatch (CCM) who can undergo thrombectomy with the Trevo device within 6–24 hours from TLSW have better outcomes at 3 months compared to subjects treated with standard medical therapy alone. Age-adjusted CCM was defined by age ($\leq$80 or $>$80 years), baseline NIHSS (10–20 or $\geq$21) and core size (0–20 cc's in subjects older than 80 and, in subjects younger than 80, 0–30 cc's with NIHSS 10–20 and 31–50 cc with NIHSS $\geq$ 21).
Method: Prospective, randomized, multicenter, Bayesian adaptive-enrichment, open label trial with blinded endpoint assessment. Subjects were randomized in a 1:1 ratio to receive thrombectomy or medical management alone. Sequential interim analyses allowing adaptation of enrolment criteria or stopping new enrolment for futility or predicted success was planned to occur every 50 randomized patients starting at 150 to a maximum of 500 patients. The primary endpoint was the modified Rankin Scale (mRS) score at 90 days analyzed as a utility weighted score and (due to regulatory considerations) also as a dichotomized variable. The primary safety outcome was stroke-related mortality at 90 days.
Results: Trial enrolment was stopped at the DSMB's recommendation due to crossing of pre-specified probability thresholds for predicted success. Full results will be provided at the presentation.

LB1000

Official Welcome & Large Clinical Trials

PFO Closure in the Gore REDUCE Clinical Trial: Primary Results

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Background and Aims: The efficacy of patent foramen ovale (PFO) closure for secondary prevention in patients with prior cryptogenic stroke has been uncertain despite multiple randomized trials completed to date. The Gore REDUCE Clinical Study (REDUCE) aimed to establish superiority of PFO closure in conjunction with antiplatelet therapy over antiplatelet therapy alone in reducing the risk of recurrent clinical ischemic stroke or new silent brain infarct in patients who have had a cryptogenic stroke.
Method: REDUCE was a randomized, controlled, open-label trial that randomized 664 subjects with cryptogenic stroke at 63 multinational sites in a 2:1 ratio to either antiplatelet therapy plus PFO closure (with Gore® Helex® Septal Occluder or Gore® CARDIOFORM Septal Occluder) or antiplatelet therapy alone. A standardized approach to antiplatelet

therapy was defined by protocol. Subjects were prospectively followed for at least 2 and up to 5 years. Neuroimaging was required for all subjects at baseline and at 2 years or study exit.

A blinded Clinical Endpoint Committee (CEC) reviewed and adjudicated all suspected stroke, TIA, and death events. A blinded MRI core laboratory compared baseline and 2-year MRI to determine the presence of new silent brain infarction.

The two co-primary endpoints for the study were freedom from recurrent clinical ischemic stroke through at least 2 years after randomization and incidence of new brain infarct (defined as the composite of clinical ischemic stroke and silent brain infarct) through 2 years. The primary analyses were performed on the intention-to-treat population using an unadjusted log-rank test and a binomial test of subject-based proportions, respectively, with adjustment for testing multiplicity.

Clinical trial registration – URL http://clinicaltrials.gov/show/NCT00738894

Results and Conclusion: The CEC completed adjudication of all potential clinical endpoints on 17 April 2017 and the primary analysis was performed on 24 April 2017. The primary endpoint results of REDUCE will be presented