

SUPPLEMENTARY MATERIAL 3: Table shells

TABLE 1. Baseline characteristics according to treatment group. Data are number (%), mean (standard deviation) or median (interquartile range), chi-squared or Kruskal-Wallis tests will be used to make comparisons.

| | Active | Control | P |
|----------------------------------|--------|---------|---|
| Age (years) | | | |
| Sex, female | | | |
| Geographical region | | | |
| North America | | | |
| Asia | | | |
| Europe | | | |
| Other | | | |
| ICH onset to randomisation (hrs) | | | |
| Medical history | | | |
| Hypertension | | | |
| Diabetes mellitus | | | |
| Stroke | | | |
| Ischaemic heart disease | | | |
| AF (history or ECG finding) | | | |
| Smoker | | | |
| Medication history | | | |
| Antihypertensive | | | |
| Antiplatelet | | | |
| Anticoagulation | | | |
| <i>Clinical</i> | | | |
| Systolic BP (mmHg) | | | |
| Diastolic BP (mmHg) | | | |
| Pulse pressure (mmHg) | | | |
| Heart rate (bpm) | | | |

Rate-pressure product¹

NIHSS (/42)

GCS (/15)

Neuroimaging

Haematoma volume (ml)

Haematoma location

Lobar

Basal ganglia/deep

Infratentorial

Intraventricular haemorrhage

Perihaematomal oedema

Absolute (ml)

Relative²

Pre-stroke characteristics

Leukoaraiosis

Atrophy

Prior stroke lesion

ICH denotes intracerebral haemorrhage; AF, atrial fibrillation; BP, blood pressure; NIHSS, National Institute for Health stroke scale; GCS, Glasgow come scale

¹Systolic BP multiplied by heart rate

²Perihaematomal oedema to intraparenchymal haemorrhage volume ratio

TABLE 2. Treatment used to lower blood pressure, and other processes of care. Data are number (%). Chi squared tests will be used to make comparisons.

| | Treatment | Control | P |
|---|-----------|---------|---|
| Route of administration | | | |
| Oral | | | |
| Intravenous | | | |
| Transdermal | | | |
| Sublingual | | | |
| BP intervention ^ | | | |
| Target * | | | |
| ACE-I, po/sl § | | | |
| ARA, po + | | | |
| β-RA, po/im §§ | | | |
| CCB, iv ¥ | | | |
| CCB, po \$ | | | |
| Nitrate, topical # | | | |
| Magnesium, iv ∫ | | | |
| Other treatments (%) | | | |
| Mannitol | | | |
| Haemostatic agents | | | |
| VTE prophylaxis | | | |
| DNAR order/withdrawal of active treatment | | | |
| ITU/intubation | | | |
| Neurosurgery | | | |

BP denotes blood pressure; ACE-I, angiotensin converting enzyme inhibitor; ARA, angiotensin receptor antagonist; β-RA, beta receptor antagonist; CCB, calcium channel blocker; VTE, venous thromboembolism; DNAR, do not attempt resuscitation; ITU, intensive treatment unit; po, oral; sl, sublingual; im, intramuscular; iv, intravenous

^ Categorized according to current BASC collaborator trials

*INTERACT1&2, ATACH-II, ICH-ADAPT; § CHHIPS, ACEi arm; + SCAST; §§ CHHIPS, β-RA arm; ¥ ATACH-II, Uzuner; \$ VENUS; # GTN1&2, ENOS, RIGHT; ∫ IMAGES, FAST-Mag

TABLE 3. Effect of BP lowering on outcomes. Data are number (%), mean (standard deviation) or median (interquartile range); mean difference (MD) or odds ratios (OR) with 95% confidence intervals (CI). Generalised linear mixed models for binary, continuous and ordinal outcomes, with random intercept for source trial. Multivariable analyses adjusted for age, sex, severity (NIHSS), systolic BP, ICH volume, presence of IVH and time to randomisation.

| | N | Treatment | Control | OR/MD | 95% CI | P | OR/MD | 95% CI | P |
|---|---|-----------|---------|------------|--------|---|----------|--------|---|
| | | | | Unadjusted | | | Adjusted | | |
| On treatment outcomes | | | | | | | | | |
| <i>Within 1 hour of randomisation</i> | | | | | | | | | |
| Systolic BP (mmHg) | | | | | | | | | |
| Mean ¹ | | | | MD | | | MD | | |
| Delta ² | | | | MD | | | MD | | |
| Peak ³ | | | | MD | | | MD | | |
| Standard deviation ⁴ | | | | MD | | | MD | | |
| Diastolic BP § (mmHg) | | | | MD | | | MD | | |
| Pulse pressure § (mmHg) | | | | MD | | | MD | | |
| Heart rate § (bpm) | | | | MD | | | MD | | |
| Rate pressure product ⁵ | | | | MD | | | MD | | |
| <i>Within 24 hours of randomisation</i> | | | | | | | | | |
| Systolic BP (mmHg) | | | | | | | | | |

| | | |
|------------------------------------|----|----|
| Mean ¹ | MD | MD |
| Delta ² | MD | MD |
| Peak ³ | MD | MD |
| Standard deviation ⁴ | MD | MD |
| Diastolic BP § (mmHg) | MD | MD |
| Pulse pressure § (mmHg) | MD | MD |
| Heart rate § (bpm) | MD | MD |
| Rate pressure product ⁵ | MD | MD |
| Neurologic deterioration | OR | OR |
| Symptomatic hypotension | OR | OR |

Within 7 days of randomisation

| | | |
|---------------------------------|----|----|
| Systolic BP (mmHg) | | |
| Mean ¹ | MD | MD |
| Delta ² | MD | MD |
| Peak ³ | MD | MD |
| Standard deviation ⁴ | MD | MD |
| Diastolic BP § (mmHg) | MD | MD |
| Pulse pressure § (mmHg) | MD | MD |
| Heart rate § (bpm) | MD | MD |

| | | |
|------------------------------------|----|----|
| Rate pressure product ⁵ | MD | MD |
| Neurologic deterioration | OR | OR |
| Symptomatic hypotension | OR | OR |

Repeat brain imaging

| | | |
|------------------------------|----|----|
| Completed within 48 hours | OR | OR |
| Haematoma volume | | |
| Absolute (ml) | MD | MD |
| Expansion | | |
| >33% | OR | OR |
| >6ml | OR | OR |
| Perihaematomal oedema volume | | |
| Absolute (ml) | MD | MD |
| Relative ⁶ | MD | MD |
| Mass effect | OR | OR |

90-day clinical outcomes

| | | |
|---|----|----|
| Primary outcome (unfavourable shift in ordinal mRS score) | OR | OR |
| Death (%) | OR | OR |

| | | |
|-------------------------------------|----|----|
| Dichotomised mRS score | | |
| 4-6, death and major disability (%) | OR | OR |
| 3-6, death and dependency (%) | OR | OR |
| Barthel index (/100) | MD | MD |
| EQ-5D-5L (/25) | MD | MD |
| MMSE (/30) | MD | MD |
| Serious adverse events | | |
| Fatal | OR | OR |
| Non-fatal | OR | OR |
| Renal | OR | OR |
| Cardiac | OR | OR |
| Pneumonia | OR | OR |
| VTE | OR | OR |

BP denotes blood pressure; SD, standard deviation; bpm, beats per minute; mRS, modified Rankin Scale; EQ-5D-5L, European Quality of Life–5

Dimensions 5-level questionnaire; MMSE, mini mental state examination; VTE, venous thromboembolism.

¹Mean of measures within specified period

²Baseline minus mean within specified period

³Highest value within specified period

⁴Standard deviation of measures within specified period

⁵Peak systolic BP multiplied by peak heart rate within specified period

§Mean, delta, peak and standard deviation will also be assessed

FIGURE 1. Shift in mRS according to BP lowering vs. control/guideline treatment. Give adjusted odds ratio from generalised linear mixed model with source trial as random effect. Adjusted for age, sex, severity (NIHSS), systolic BP, ICH volume at baseline, IVH at baseline, time to randomisation.

FIGURE 2. Forest plot of shift in mRS by pre-defined subgroups. Same model as figure 1 with interaction tests.

- Age: ≤ 70 , >70 (years)
- Sex
- Region: Asian vs other
- Pre-stroke hypertension: Y/N
- Pre-stroke antithrombotic use: Y/N
- Baseline SBP: ≤ 140 , 140-180, 180-220, >220 (mmHg)
- NIHSS: ≤ 8 , 9-15, >15
- Haematoma volume at baseline: ≤ 15 , >15 (ml)
- Type of intervention: target vs angiotensin inhibitor vs CCB vs NO donor vs magnesium/other
- Time from stroke to randomisation: <2 , 2-6, 6-48, >48 (hours)
- Type of trial: pre-hospital vs hospital, ICH only vs mixed

FIGURE 3. Kaplan-Meier curve for death with comparison of active and control treatment groups. Model adjusted for age, sex, severity (NIHSS), systolic BP, ICH volume at baseline, IVH at baseline, time to randomisation and source trial.

FIGURE 4. Forest plot for end-of-trial death by pre-defined subgroups. Same model as figure 1 with interaction tests.

- Age: ≤ 70 , >70 (years)
- Sex
- Region: Asian vs other
- Pre-stroke hypertension: Y/N
- Pre-stroke antithrombotic use: Y/N
- Baseline SBP: ≤ 140 , 140-180, 180-220, >220 (mmHg)
- NIHSS: ≤ 8 , 9-15, >15
- Haematoma volume at baseline: ≤ 15 , >15 (ml)
- Type of intervention: target vs angiotensin inhibitor vs CCB vs NO donor vs magnesium/other
- Time from stroke to randomisation: <2 , 2-6, 6-48, >48 (hours)
- Type of trial: pre-hospital vs hospital, ICH only vs mixed

FIGURE 5. Individual participant data regression: relationship between randomised treatment group and odds ratio for unfavourable shift in scores on the modified Rankin Scale at end of trial and (i) time to randomisation; (ii) baseline systolic blood pressure; and (iii) baseline haematoma volume. Model (i) is adjusted for age, sex, severity, type of treatment, and source trial; models (ii) and (iii) are adjusted for the same plus time to randomisation.