

SUPPLEMENTAL MATERIAL

Includes Figures e1 to e4 and eAppendix

Effect of IV alteplase on the ischemic brain lesion at 24-48 hours after ischemic stroke

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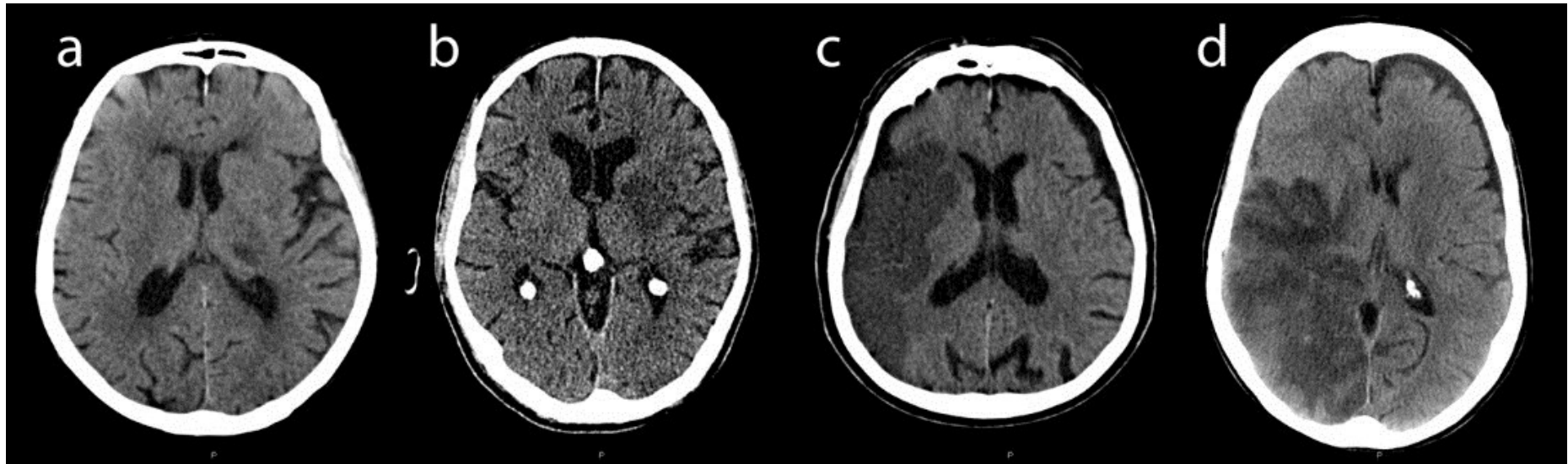
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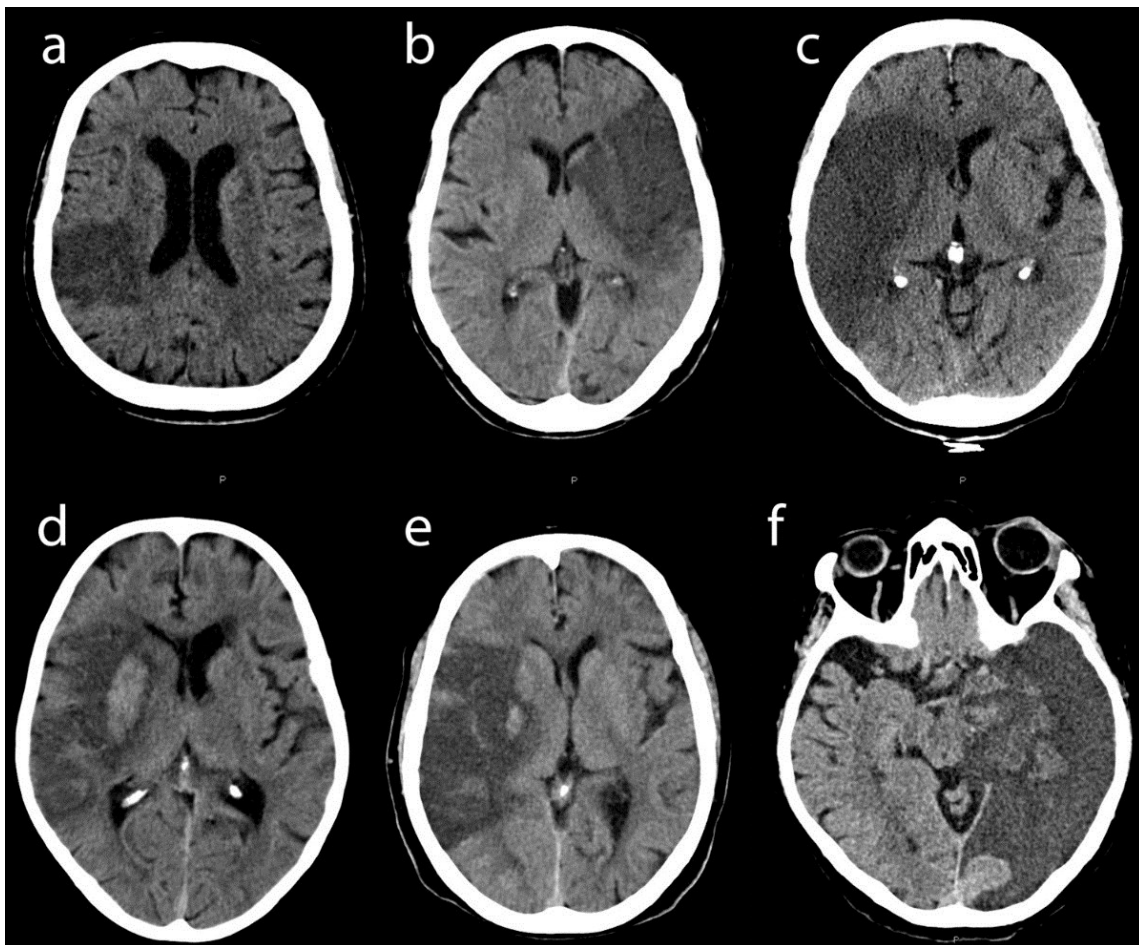
Figure e1. IST-3 Ischemic Lesion Score examples



Footnote:

- a) Lacunar lesion within the left thalamus, IST-3 score = 1
- b) Lesion within the left lentiform nucleus, >2cm, IST-3 score = 2
- c) Lesion affecting the entire right middle cerebral artery territory, IST-3 score = 3
- d) Lesion of both the right middle cerebral and right posterior cerebral arterial territories, IST-3 score = 4

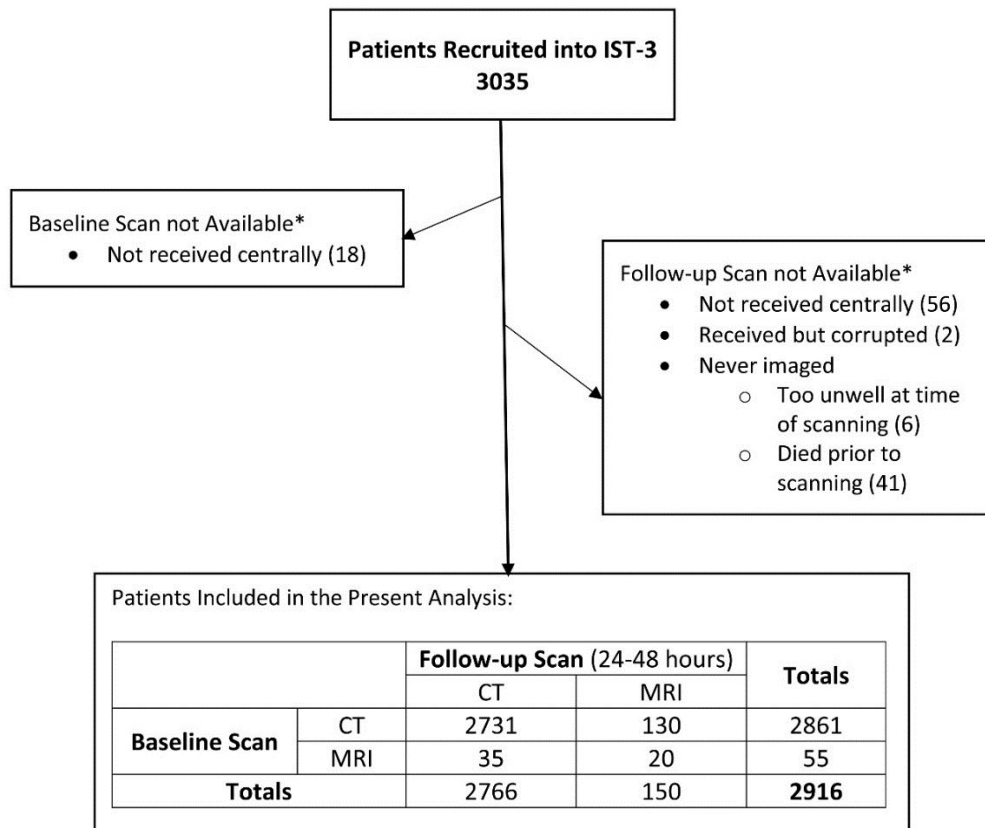
Figure e2. Grades of brain swelling within the acute lesion



Footnote:

- a) Grade 1 = effacement of sulci adjacent to ischemia
- b) Grade 2 = effacement of sulci and partial effacement of the lateral ventricle
- c) Grade 3 = effacement of sulci and complete effacement of the lateral ventricle
- d) Grade 4 = effacement of sulci and the lateral and third ventricles
- e) Grade 5 = effacement of sulci and ventricles with midline shift
- f) Grade 6 = effacement of sulci, ventricles and the basal cisterns

Figure e3. Flow chart to identify cases included in this analysis and the scan modality used for each



* Note that 4 patients had no centrally available imaging at either baseline or follow-up

Figure e4. Ordinal regression analyses to test for interactions between alteplase and clinical/imaging characteristics on change in grade of lesion visibility between baseline and 24-48 hour (dependent variable), n=2916.

Variable	Subgroups (n)	Odds Ratio (95% CI), p-value		p-value for Interaction
NIHSS	0-7 (963)	1.29 (1.01-1.65)	0.043	0.842
	8+ (1953)	1.33 (1.12-1.58)	0.001	
Leukoaraiosis	Yes (1489)	1.31 (1.08-1.60)	0.006	0.871
	No (1427)	1.28 (1.05-1.56)	0.013	
Atrophy	Yes (2245)	1.25 (1.07-1.47)	0.005	0.358
	No (671)	1.46 (1.09-1.95)	0.011	
Old Stroke Lesion(s)	Yes (1304)	1.19 (0.97-1.47)	0.096	0.239
	No (1612)	1.41 (1.16-1.70)	<0.001	

Favours Control Favours Alteplase

Footnote:

Odds Ratio (OR) relates to the impact of alteplase on the likelihood of developing a more visible lesion on follow-up imaging.

OR>1 (right of vertical line) indicates alteplase is protective against increased lesion visibility.

NIHSS = National Institutes of Health Stroke Scale. CI = Confidence Interval.

Adjusted for age, NIHSS, atrophy, leukoaraiosis, old stroke lesion, interval between scans, hemorrhage on follow-up scan.

eAppendix. Funding sources for IST-3

The start-up phase of IST-3 was supported by a grant from the Stroke Association, UK (TSA 04/99). The expansion phase was funded by the Health Foundation UK (2268/1282). The scan reading development was funded by Chest, Heart Stroke Scotland (R100/7).

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Boehringer-Ingelheim GmbH donated drug and placebo for the 300 patients in the double-blind phase, but thereafter had no role whatsoever in the trial.

The UK Stroke Research Network (SRN study ID 2135) adopted the trial in 01/05/2006, supported the initiation of new UK sites, and in some centres, and, after that date, data collection was undertaken by staff funded by the network or working for associated NHS organisations.

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