Table S1 Comparison of characteristics of patients recruited from UK and outside UK

Characteristics	**UK**	**Non-UK**	**P**
Age	69.7 (13.7)	65.1 (13.8)	<0.001
Sex, male	1041 (54.5)	260 (62.7)	0.002
Premorbid modified Rankin Scale	0 [0, 1]	0 [0, 0]	<0.001
NIHSS	12 [6, 19]	12 [8, 18]	0.92
Prior antiplatelet therapy	518 (27.1)	93 (22.4)	0.048
Systolic blood pressure	174.6 (30.6)	175.5 (27.2)	0.57
Previous ischemic stroke/TIA	250 (13.2)	80 (19.4)	0.001
Previous intracerebral hemorrhage	112 (5.9)	14 (3.4)	0.041
Ischemic heart disease	172 (9.1)	31 (7.5)	0.29
Hypertension	1105 (58.3)	316 (76.1)	<0.001
Diabetes mellitus	251 (13.2)	61 (14.7)	0.41
Atrial fibrillation	53 (2.8)	18 (4.3)	0.096
Onset-to-CT time (hours)	2.3 (1.3)	2.2 (1.4)	0.32
Onset-to-randomization (hours)	3.8 (1.6)	4.5 (1.9)	<0.001
Brief consent	558 (29.2)	25 (6.0)	<0.001
Lobar hematoma	605 (32.2)	83 (20.6)	<0.001
Intraventricular hemorrhage	611 (32.3)	96 (23.8)	0.001
Hematoma volume (mL)	25.3 (27.8)	17.8 (22.9)	<0.001
Management within the first week			
Treated with tranexamic acid	254 (49.9)	207 (49.9)	0.98
Invasive ventilation	130 (6.8)	36 (8.7)	0.18
Intensive care	192 (10.1)	40 (9.7)	0.80
DNAR	471 (24.8)	38 (9.2)	<0.001
Neurosurgery	95 (5.0)	26 (6.3)	0.28
Day 90 outcome			
Modified Rankin Scale of 4-6	1073 (56.7)	186 (44.8)	<0.001
Death	422 (22.3)	77 (18.6)	0.093

Data are number (%), median [interquartile range] or mean (standard deviation). Statistics are t-Student, Mann-Whitney U and Chi-squared test. DNAR=do not attempt resuscitation; NIHSS=National Institutes of Health Stroke Scale; TIA=transient ischemic attack

Table S2 Logistic regression analyses for predictors of neurological deterioration excluding patients with DNAR order

Variables	Early neurological deterioration[a]		Late neurological deterioration[b]	
	Adjusted OR (95%CI)	P	Adjusted OR (95%CI)	P
Age (years)	0.997 (0.983-1.012)	0.73	1.023 (1.001-1.045)	0.043
Sex (male)	1.20 (0.895-1.68)	0.31	1.32 (0.78-2.21)	0.30
Country (UK)	1.91 (1.23-3.05)	0.004	1.08 (0.61-1.92)	0.80
Premorbid modified Rankin Scale	1.03 (0.87-1.24)	0.71	0.96 (0.74-1.25)	0.77
Systolic blood pressure (mmHg)	1.007 (1.001-1.012)	0.017	1.002 (0.993-1.010)	0.70
National Institute of Health Stroke Scale	1.04 (1.01-1.07)	0.009	1.05 (1.00-1.09)	0.033
Onset-to-CT time (hours)	0.83 (0.72-0.96)	0.011	0.98 (0.81-1.19)	0.82
Previous antiplatelet therapy	1.49 (1.01-2.20)	0.043	1.17 (0.66-2.08)	0.59
Previous intracerebral hemorrhage	2.74 (1.44-5.19)	0.002	2.66 (1.04-6.80)	0.041
Intraventricular hemorrhage	1.46 (1.02-2.08)	0.041	1.67 (0.99-2.79)	0.052
Subarachnoid extension	2.13 (1.35-3.37)	0.001	0.86 (0.36-2.04)	0.73
Lobar location	1.50 (0.95-2.35)	0.079	1.08 (0.52-2.23)	0.84
Hematoma volume (per 10 mL increase)	1.18 (1.05-1.32)	<0.001	1.22 (1.04-1.42)	0.012
PHE volume (per 10 mL increase)	1.10 (0.94-1.28)	0.095	0.95 (0.74-1.23)	0.72
Midline shift ≥5mm	1.93 (1.19-3.13)	0.008	2.25 (1.17-4.33)	0.015
Leukoaraiosis	1.35 (0.95-1.94)	0.099	1.00 (0.59-1.69)	0.99
Raised leukocyte count (>11.0 $X10^9$/L)	1.09 (0.72-1.66)	0.68	1.43 (0.80-2.55)	0.23
Glucose (mmol/L)	1.01 (0.96-1.07)	0.67	1.03 (0.95-1.11)	0.54

All variables significant on univariate analysis were entered into the models. PHE=perihematomal edema. [a]Excluding patients with DNAR order at day 2; [b]excluding patients with DNAR order at day 7.

Table S3 Effect of tranexamic acid on neurological deterioration, serious adverse events and radiological outcomes excluding patients with DNAR order

	Tranexamic acid	Placebo	MD/OR (95%CI)	p
Neurological deterioration[a]				
All ≤7 days	163 (18.2)	199 (22.0)	0.76 (0.59, 0.99)	0.039
Early (<48 hours)	155 (17.1)	177 (19.8)	0.75 (0.57, 0.98)	0.034
Late (48 hours to 7 days)	41 (5.3)	51 (6.7)	0.78 (0.52, 1.19)	0.25
SAE with neurological deterioration ≤7 days[b]				
Cerebral events	147 (15.3)	177 (18.5)	0.80 (0.63, 1.01)	0.062
Non-cerebral events	25 (2.6)	28 (2.9)	0.89 (0.51, 1.53)	0.67
Radiological outcomes[a]				
Hematoma expansion	200 (22.5)	20 (26.0)	0.76 (0.61, 0.96)	0.019
Haematoma progression	314 (32.8)	375 (39.2)	0.69 (0.56,0.85)	0.001
PHE growth (mL)	5.9 (9.8)	5.7 (11.2)	-0.031 (-0.95, 0.88)	0.95

Hematoma expansion was defined as an increase in hematoma volume of >33% or >6mL on follow-up scan compared to baseline. Perihematomal edema (PHE) growth is the absolute difference in PHE volume between follow-up and baseline scans. [a]Adjusted for age, sex, country of recruitment, systolic blood pressure, previous antiplatelet therapy, National Institute of Health Stroke Scale, onset to randomisation time, intraventricular hemorrhage and baseline hematoma volume. [b]Unadjusted. Patient with DNAR order at day 2 excluded from analyses of early neurological deterioration and radiological outcomes; patient with DNAR order at day 7 excluded from analyses of late neurological deterioration and neurological deterioration ≤7 days. MD=mean difference; OR=odds ratio; SAE=serious adverse event

Table S4 Serious adverse event classification of early and late neurological deterioration

Serious adverse event classification	**END (n=590)**	**LND (n=145)**	**Total (n=735)**
Not reported	47 (8.0)	28 (19.3)	75 (10.2)
Not serious adverse event	5 (0.8)	4 (2.8)	9 (1.2)
Not relevant, > 7days	-	1 (0.7)	1 (0.1)
Cerebral events	499 (84.6)	79 (54.5)	578 (78.6)
Expansion of haemorrhagic stroke	256 (43.4)	17 (11.7)	273 (37.1)
Neurological deterioration (Cause not specified)	138 (23.4)	28 (19.3)	166 (22.6)
Cerebral edema	41(6.9)	16 (11.0)	57 (7.8)
Hydrocephalus	29 (4.9)	6 (4.1)	35 (4.8)
Seizure	20 (3.4)	8 (5.8)	28 (3.8)
Sedation	6 (1.1)	1 (0.7)	7 (1.0)
Recurrent intracerebral hemorrhage	4 (0.7)	-	4 (0.5)
Ischemic stroke	3 (0.5)	2 (1.4)	5 (0.7)
Transient ischemic attack	-	1 (0.7)	1 (0.1)
Stroke undetermined	1 (0.2)	-	1 (0.1)
Loss of consciousness	1 (0.2)	-	1 (0.1)
Non-cerebral events	39 (6.6)	33 (22.8)	72 (9.8)
Pneumonia/chest infection/LRTI	29 (4.9)	22 (15.1)	51 (6.9)
STEMI/NSTEMI	2 (0.4)	-	2 (0.3)
Pulmonary embolism	1 (0.2)	1 (0.7)	2 (0.3)
Infection (not otherwise specified)	1 (0.2)	1 (0.7)	2 (0.3)
Urinary tract infection	1 (0.2)	2 (1.4)	3 (0.4)
Exacerbation of COPD	1 (0.2)	-	1 (0.1)
Fall	1 (0.2)	-	1 (0.1)
Fatigue	1 (0.2)	-	1 (0.1)
Hypotension	1 (0.2)	-	1 (0.1)
Alcohol withdrawal	1 (0.2)	1 (0.7)	2 (0.3)
Malignancy	-	2 (1.4)	2 (0.3)
Cardiac failure/pulmonary edema	-	2 (1.4)	2 (0.3)
Electrolyte imbalance	-	1 (0.7)	1 (0.1)
Anaemia	-	1 (0.7)	1 (0.1)

COPD=chronic obstructive pulmonary disease; END= early neurological deterioration; LND= late neurological deterioration; LRTI=lower respiratory tract infection; STEMI/NSTEMI=ST elevation myocardial infarction/Non-ST elevation myocardial infarction

Table S5 Effect of early neurological deterioration on day 90 outcome

Outcomes	**Early Neurological deterioration**	**No neurological deterioration**	**OR/MD 95% CI***	**P**
Day 7, death	196 (33.2)	9 (0.6)	41.97 (20.33, 86.62)	<0.001
Day 90				
Death	315 (53.8)	117 (7.5)	8.80 (6.40, 12.10)	<0.001
mRS>3	513 (87.5)	618 (39.4)	5.18 (3.72, 7.22)	<0.001
Barthel Index	16.5 (34.0)	69.9 (37.2)	-29.5 (-32.6, -26.3)	<0.001
EQ5D HUS	0.08 (0.27)	0.46 (0.39)	-0.19 (-0.23, -0.16)	<0.001
TICS	1.9 (7.8)	20.1 (10.0)	-9.9 (-11.1, -8.7)	<0.001
ZDS	94.1 (21.0)	53.6 (23.5)	22.2 (19.2, 25.2)	<0.001

*Adjusted for age, sex, country of recruitment, previous antiplatelet therapy, National Institute of Health Stroke Scale, systolic blood pressure, onset to randomization time, baseline haematoma volume, intraventricular haemorrhage and treatment with tranexamic acid. EQ5D HUS=EuroQoL-5D Health Utility Scores; MD=mean difference; mRS=modified Rankin Scale; OR= odds ratio; TICS=Telephone Interview Cognitive Status; ZDS= Zung Depression Scale

Table S6 Effect of late neurological deterioration on day 90 outcome

Outcomes	Late neurological deterioration	No neurological deterioration	OR/MD 95% CI*	P
Day 7, death	18 (12.4)	9 (0.6)	9.70 (3.49, 26.96)	<0.001
Day 90				
Death	65 (44.8)	117 (7.5)	6.00 (3.71, 9.70)	<0.001
mRS>3	123 (84.8)	618 (39.4)	4.06 (2.35, 7.03)	<0.001
Barthel Index	21.8 (37.4)	69.9 (37.2)	-24.8 (-30.0, -19.7)	<0.001
EQ5D HUS	0.12 (0.29)	0.46 (0.39)	-0.15 (-0.21, -0.09)	<0.001
TICS	2.9 (8.8)	20.1 (10.0)	-8.5 (-10.4, -6.5)	<0.001
ZDS	91.0 (24.6)	53.6 (23.5)	19.0 (14.0, 24.0)	<0.001

* Adjusted for age, sex, country of recruitment, previous antiplatelet therapy, National Institute of Health Stroke Scale, systolic blood pressure, onset to randomization time, baseline haematoma volume, intraventricular haemorrhage and treatment with tranexamic acid. EQ5D HUS=EuroQoL-5D Health Utility Scores; MD=mean difference; mRS=modified Rankin Scale; OR= odds ratio; TICS=Telephone Interview Cognitive Status; ZDS= Zung Depression Scale