EMERGING THERAPY IN STROKE MEDICINE

7th MAR 2018

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North-Eastern Stroke Research Group

Outline

- Thrombolytic therapy
- Mechanical Thrombectomy
- Antiplatelet drug
- Anticoagulant drug
- Other management

Outline

- **Thrombolytic therapy**
- Mechanical Thrombectomy
- Antiplatelet drug
- Anticoagulant drug
- Other management

Thrombolytic therapy

- 1st generation
  - *Streptokinase, Urokinase*
- 2nd generation
  - *Prourokinase*
  - *Alteplase (r-tPA)** (NIND, ECLASSIII ,etc. FDA approved for IV)*
- 3rd & 4th generation
  - *Staphylokinase, Reteplase, Monteplase,*
  - *Lanoteplase, Ancrod*
  - ***Desmoteplase, Tenecteplase***

Desmoteplase vs Placebo

Stroke

Intravenous desmoteplase in patients with acute ischaemic stroke selected by MRI perfusion-diffusion weighted imaging or perfusion CT (DIAS-2): a prospective, randomised, double-blind, placebo-controlled study

Safety and efficacy of desmoteplase given 3-9 h after ischaemic stroke in patients with occlusion or high-grade stenosis in major cerebral arteries (DIAS-3): a double-blind, randomised, placebo-controlled phase 3 trial

Stroke

Desmoteplase 3 to 9 Hours After Major Artery Occlusion Stroke: The DIAS-4 Trial (Efficacy and Safety Study of Desmoteplase to Treat Acute Ischemic Stroke)

Desmoteplase in Acute Ischemic Stroke (DIAS)

- Extended time window to 3-9 hr
- Desmoteplase or placebo, given as a single iv bolus injection.

desmoteplase was beneficial for pts w/ proximal arterial occlusion

Pt w/ perfusion/diffusion mismatch is associated with a higher rate of reperfusion and better clinical outcome than placebo

supported an excellent safety profile with the 90 µg/kg dose.

Phase III study
- Japanese pts
- Asia and Europe
- North and Latin America and Europe

DIAS
DEDAS
2005

DIAS-2
2009

DIAS-J
DIAS-3
DIAS-4
2015 2016

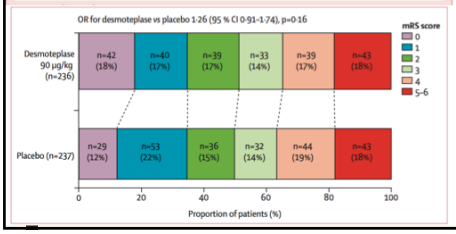
Safety and efficacy of desmoteplase given 3–9 h after ischaemic stroke in patients with occlusion or high-grade stenosis in major cerebral arteries (DIAS-3): a double-blind, randomised, placebo-controlled phase 3 trial

Gregory W Albers*, Rüdiger von Kummer*, Thomas Truelsen, Jens-Kristian S Jensen, Gabriela M Ravn, Bjørn A Grønning, Hugues Chabriat, Ku-Chou Chang, Antonio E Davalos, Gary A Ford, James Grotta, Markku Kaste, Lee H Schwamm, Ashfaq Shuaib, for the DIAS-3 Investigators†

Summary

Background Current treatment of ischaemic stroke with thrombolytic therapy is restricted to 3–4·5 h after symptom

	Placebo group	Desmoteplase group	Odds ratio (95% CI)	p value
Primary endpoint				
mRS response (scores 0–2) at 90 days*†	118/237 (50%)	121/236 (51%)	1·20 (0·79–1·81)	0·40



DIAS-3 desmoteplase was as safe as placebo, but without clinical benefit.

Terminated the DIAS-4 trial after the enrollment of 270/400 pts, because the goal of 2 positive trials could not be met.

Stroke

American Heart Association | American Stroke Association

Desmoteplase 3 to 9 Hours After Major Artery Occlusion Stroke: The DIAS-4 Trial (Efficacy and Safety Study of Desmoteplase to Treat Acute Ischemic Stroke)

Rüdiger von Kummer Prof Dr med, Etsuro Mori, Thomas Truelsen, Jens-Kristian S. Jensen, Bjørn A. Grønning, Jochen B. Fiebach Prof Dr med, Karl-Olof Lovblad Prof Dr med, Salvador Pedraza, Javier M. Romero, Hugues Chabriat, Ku-Chou Chang, Antoni Dávalos, Gary A. Ford, James Grotta, Markku Kaste, Lee H. Schwamm, Ashfaq Shuaib and Gregory W. Albers for the DIAS-4 Investigators

Stroke. 2016;47:2880-2887; originally published online November 1, 2016;

Pooled DIAS-3, DIAS-4, and DIAS-J patient data

	Treatment	N	n (%)	OR (95% CI)	*P* Value
Primary end point					
mRS 0–2 response	Placebo	128	46 (35.9)		
	DSPA	124	52 (41.9)	1.45 (0.79–32.64)	0.2290
Recanalization at 12–24 h					
Patients with TIMI score 0–1 at baseline who had a 12–24 h follow-up with CTA/MRA	Placebo	58	17 (29.3)		
	DSPA	48	25 (52.1)	2.66 (1.17–6.06)	0.0198

Desmoteplase is safe, increases arterial recanalization, but does not significantly improve functional outcome at 3 months.

Desmoteplase

- Desmoteplase in 3-9hr of AIS onset
  - Not significantly improve functional outcome at 3 months compare to placebo
  - Increases arterial recanalization: pts with major cerebral artery occlusions and a small ischemic core seems to be a relevant target for more effective means for arterial recanalization beyond 3 hours
  - Waiting for further study?

Tenecteplase vs Alteplase

Stroke

American Heart Association | American Stroke Association

Phase IIB/III Trial of Tenecteplase in Acute Ischemic Stroke: Results of a Prematurely Terminated Randomized Clinical Trial

E. Clarke Haley Jr, John J. P. Thompson, James C. Grotta, Patrick D. Lyden, Thomas G. Hemmen, Devin Brown, Rafael H. Llinas, ...

Stroke

THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Randomized Trial of Tenecteplase versus Alteplase for Acute Ischemic Stroke

Mark Parsons, M.D., Neil Spratt, M.D., Andrew Bivard, B.Sc., ...

Bruce
Bill O'E
Chris

Alteplase versus tenecteplase for thrombolysis after ischaemic stroke (ATTEST): a phase 2, randomised, open-label, blinded endpoint study

Xuya Huang, Bharath Kumar Cheripelli, Suzanne M Lloyd, Dheeraj Kalladka, Fiona Catherine Moreton, Aslam Siddiqui, Ian Ford, Keith W Muir

Lancet Neurol 2015; 14: 368–

Tenecteplase versus alteplase for management of acute ischaemic stroke (NOR-TEST): a phase 3, randomised, open-label, blinded endpoint trial

Nicola Logallo, Wojtech Novotny, Jörg Assmus, Christopher E Kvistad, Lars Alteheld, Ole Morten Rønning, Bente Thommessen, Karl-Friedrich Amthor, Hege Pihl-Hansen, Martin Kurz, Håkon Tobro, Kamaljit Kaur, Magdalena Stankiewicz, Maria Carlsson, Åse Morsund, Titto Idicula, Anne Hege Aamodt, Christian Lund, Halvor Næss, Ulrike Waje-Andreassen, Lars Thomassen

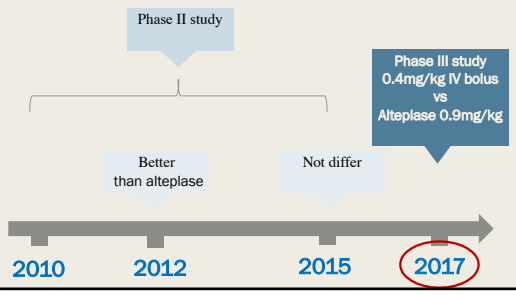
Summary

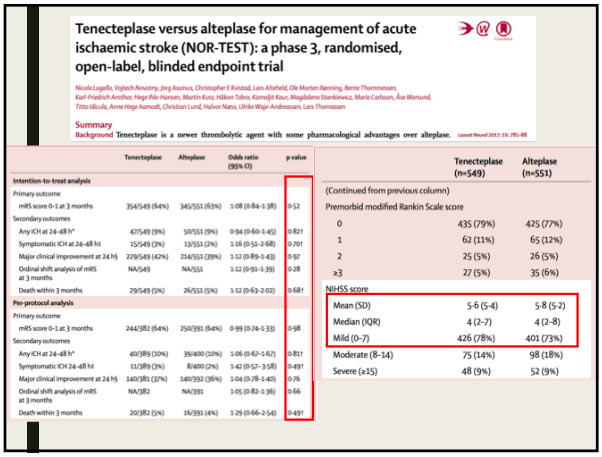
Background Tenecteplase is a newer thrombolytic agent with some pharmacological advantages over alteplase.

Lancet Neurol 2012; 11: 781–88

Tenecteplase vs Alteplase

- Time window to 4.5 hr
- Tenecteplase or Alteplase
- Teneteplase given as a single iv bolus injection.





	Tenecteplase	Alteplase	Odds ratio (95% CI)	p value
Intention-to-treat analysis				
Primary outcome				
mRS score 0–1 at 3 months	354/549 (64%)	345/551 (63%)	1·08 (0·84–1·38)	0·52
Secondary outcomes				
Any ICH at 24–48 h*	47/549 (9%)	50/551 (9%)	0·94 (0·60–1·45)	0·82†
Symptomatic ICH at 24–48 h‡	15/549 (3%)	13/551 (2%)	1·16 (0·51–2·68)	0·70†
Major clinical improvement at 24 h§	229/549 (42%)	214/551 (39%)	1·12 (0·89–1·43)	0·32
Ordinal shift analysis of mRS at 3 months	NA/549	NA/551	1·12 (0·91–1·39)	0·28
Death within 3 months	29/549 (5%)	26/551 (5%)	1·12 (0·63–2·02)	0·68†
Per-protocol analysis				
Primary outcome				
mRS score 0–1 at 3 months	244/382 (64%)	250/391 (64%)	0·99 (0·74–1·33)	0·98
Secondary outcomes				
Any ICH at 24–48 h*	40/389 (10%)	39/400 (10%)	1·06 (0·67–1·67)	0·81†
Symptomatic ICH 24–48 h‡	11/389 (3%)	8/400 (2%)	1·42 (0·57–3·58)	0·49†
Major clinical improvement at 24 h§	140/381 (37%)	140/392 (36%)	1·04 (0·78–1·40)	0·76
Ordinal shift analysis of mRS at 3 months	NA/382	NA/391	1·05 (0·82–1·36)	0·66
Death within 3 months	20/382 (5%)	16/391 (4%)	1·29 (0·66–2·54)	0·49†

	Tenecteplase (n=549)	Alteplase (n=551)
(Continued from previous column)		
Premorbid modified Rankin Scale score		
0	435 (79%)	425 (77%)
1	62 (11%)	65 (12%)
2	25 (5%)	26 (5%)
≥3	27 (5%)	35 (6%)
NIHSS score		
Mean (SD)	5·6 (5·4)	5·8 (5·2)
Median (IQR)	4 (2–7)	4 (2–8)
Mild (0–7)	426 (78%)	401 (73%)
Moderate (8–14)	75 (14%)	98 (18%)
Severe (≥15)	48 (9%)	52 (9%)

Tenecteplase vs Alteplase

- Tenecteplase was not superior to alteplase and showed a similar safety profile
- Most patients enrolled in this study had mild stroke.
- Further trials are needed to establish the safety and efficacy in patients with severe stroke
- Tenecteplase is given as a single IV bolus as opposed to the 1-hour infusion of alteplase

Thrombolytic therapy

AHA/ASA Guideline

2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

Reviewed for evidence-based integrity and endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons

Endorsed by the Society for Academic Emergency Medicine

1. The benefit of IV defibrinogenating agents and of IV fibrinolytic agents other than alteplase and tenecteplase is unproven; therefore, their administration is not recommended outside a clinical trial.	III: No Benefit	B-R
2. Tenecteplase administered as a 0.4-mg/kg single IV bolus has not been proven to be superior or noninferior to alteplase but might be considered as an alternative to alteplase in patients with minor neurological impairment and no major intracranial occlusion.	IIb	B-R

Outline

- Thrombolytic therapy
- Mechanical Thrombectomy
- Antiplatelet drug
- Anticoagulant drug
- Other management

Mechanical Thrombectomy

Present Criteria:

(1) Prestroke mRS score of 0 - 1

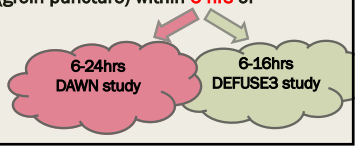
(2) Occlusion of the ICA or MCA segment 1 (M1)

(3) Age ≥18 years

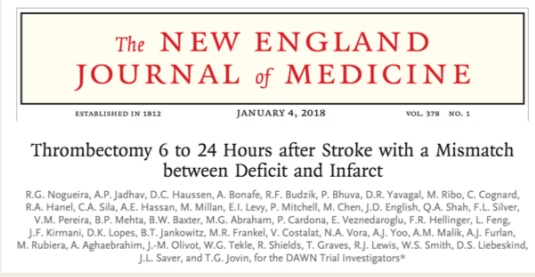
(4) NIHSS score of ≥6

(5) ASPECTS of ≥6

(6) Can be initiated (groin puncture) within 6 hrs of symptom onset



DAWN study



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 4, 2018 VOL. 378 NO. 1

Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct

R.G. Nogueira, A.P. Jadhav, D.C. Haussen, A. Bonafe, R.F. Budzik, P. Bhuva, D.R. Yavagal, M. Ribo, C. Cognard, R.A. Hanel, C.A. Sila, A.E. Hassan, M. Millan, E.I. Levy, P. Mitchell, M. Chen, J.D. English, Q.A. Shah, F.L. Silver, V.M. Pereira, B.P. Mehta, B.W. Baxter, M.G. Abraham, P. Cardona, E. Veznedaroglu, F.R. Hellinger, L. Feng, J.F. Kirmani, D.K. Lopes, B.T. Jankowitz, M.R. Frankel, V. Costalat, N.A. Vora, A.J. Yoo, A.M. Malik, A.J. Furlan, M. Rubiera, A. Aghaebrahim, J.-M. Olivot, W.G. Tekle, R. Shields, T. Graves, R.J. Lewis, W.S. Smith, D.S. Liebeskind, J.L. Saver, and T.G. Jovin, for the DAWN Trial Investigators*

- A multicenter, prospective, randomized, open-label trial with a Bayesian adaptive–enrichment design
- Compared endovascular therapy plus standard medical therapy with standard medical therapy alone in patients with AIS (6-24hr)

N Engl J Med 2018;378:11-21.

Inclusion criteria

- Occlusion of ICA/M1 on CTA/MRA
- Mismatch between the severity of the clinical deficit and the infarct volume, following criteria:
  - *Group A >= 80 yrs, NIHSS >=10, infarct volume < 21ml*
  - *Group B < 80 yrs, NIHSS >=10, infarct volume < 31ml*
  - *Group C < 80 yrs, NIHSS >=20, infarct volume 31-<51ml*
- Last seen normal 6-24hrs
- Age >= 18 yrs
- Prestroke mRS 0-1
- No ICH
- no evidence of an infarct > 1/3 of MCA
- Late presentation or received treatment with iv alteplase and had persistent occlusion of the vessel at the time that they were eligible for enrollment in the trial

Table 1. Characteristics of the Patients at Baseline.*

Trevo

Variable	Thrombectomy Group (N=107)	Control Group (N=99)
Age — yr	69.4±14.1	70.7±13.2
Age ≥80 yr — no. (%)	25 (23)	29 (29)
Male sex — no. (%)	42 (39)	51 (52)
Atrial fibrillation — no. (%)	43 (40)	24 (24)
Diabetes mellitus — no. (%)	26 (24)	31 (31)
Hypertension — no. (%)	83 (78)	75 (76)
Previous ischemic stroke or transient ischemic attack — no. (%)	12 (11)	11 (11)
NIHSS score†		
Median	17	17
Interquartile range	13–21	14–21
10 to 20 — no. (%)	78 (73)	72 (73)
Treatment with intravenous alteplase — no. (%)	5 (5)	13 (13)
Occlusion site — no. (%)§		
Intracranial internal carotid artery	22 (21)	19 (19)
First segment of middle cerebral artery	83 (78)	77 (78)
Second segment of middle cerebral artery	2 (2)	3 (3)
Interval between time that patient was last known to be well and randomization — hr		
Median	12.2	13.3

ICA/M1

6-24 hr

Table 1. Characteristics of the Patients at Baseline.*

Variable	Thrombectomy Group (N=107)	Control Group (N=99)
Infarct volume — ml		
Median	7.6	8.9
Interquartile range	2.0–18.0	3.0–18.1
Type of stroke onset — no. (%)‡		
On awakening	67 (63)	47 (47)
Unwitnessed stroke	29 (27)	38 (38)
Witnessed stroke	11 (10)	14 (14)

DWI (MRI) or CTP automated software (RAPID,iSchemaView)

Mean score for disability on the utility-weighted modified Rankin scale at 90 days.

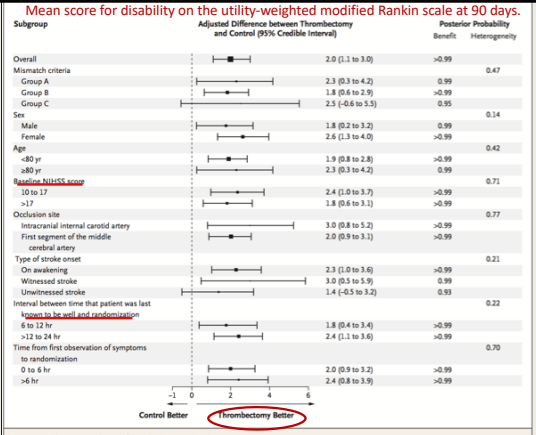


Figure 2. Subgroup Analyses of the First Primary End Point.

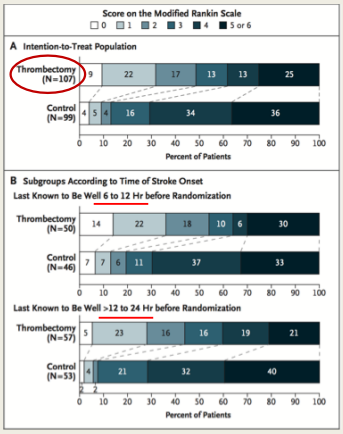


Table 3. Safety Outcomes.*

Outcome	Thrombectomy Group (N=107)	Control Group (N=99)	Absolute Difference (95% CI)	Risk Ratio (95% CI)
	no. (%)		percentage points	
Stroke-related death at 90 days	17 (16)	18 (18)	−2 (−13 to 8)	1 (1 to 2)
Death from any cause at 90 days	20 (19)	18 (18)	1 (−10 to 11)	1 (1 to 2)
Symptomatic intracranial hemorrhage at 24 hr†	6 (6)	3 (3)	3 (−3 to 8)	2 (1 to 7)
Neurologic deterioration at 24 hr‡	15 (14)	26 (26)	−12 (−23 to −1)	1 (0 to 1)
Procedure-related complications	7 (7)	NA		
Distal embolization in a different territory	4 (4)	NA		
Intramural arterial dissection	2 (2)	NA		
Arterial perforation	0	NA		
Access-site complications leading to intervention	1 (1)	NA		

* There were no significant differences between the two treatment groups with respect to safety outcomes, except for neurologic deterioration (P=0.04). All safety outcomes were adjudicated by an independent clinical-events committee.

DAWN study

- Patients with AIS who had last been known to be well 6 to 24 hrs earlier and who had a mismatch between clinical deficit and infarct, outcomes for disability at 90 days were better with thrombectomy plus standard care than with standard care alone.

N Engl J Med 2018;378:11-21.

DEFUSE3 study

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging

G.W. Albers, M.P. Marks, S. Kemp, S. Christensen, J.P. Tsai, S. Ortega-Gutierrez, R.A. McTaggart, M.T. Torbey, M. Kim-Tenser, T. Leslie-Mazwi, A. Sarraj, S.E. Kasner, S.A. Ansari, S.D. Yeatts, S. Hamilton, M. Mlynash, J.J. Heit, G. Zaharchuk, S. Kim, J. Carrozzella, Y.Y. Palesch, A.M. Demchuk, R. Bammer, P.W. Lavori, J.P. Broderick, and M.G. Lansberg, for the DEFUSE 3 Investigators*

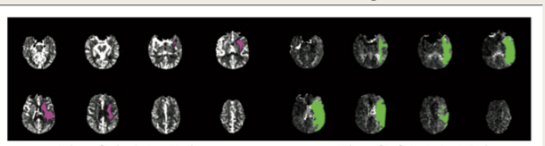
This article was published on January 24, 2018, and updated on February 16, 2018, at NEJM.org.

N Engl J Med 2018;378:708-18.
DOI: 10.1056/NEJMoa1713973

- A randomized, open-label trial with blinded outcome assessment.
- Compared endovascular therapy plus standard medical therapy with standard medical therapy alone in patients with AIS (6-16 hrs)

Inclusion criteria

- Occlusion of cervical or intracranial ICA/M1 on CTA/MRA
- CTP or MRI diffusion and perfusion scans were calculated with the use of RAPID software (iSchemaView) shown:
  - *initial infarct volume (ischemic core) of less than 70 ml*
  - *a ratio of volume of ischemic tissue to initial infarct volume of 1.8 or more*
  - *Penumbra >= 15ml (estimated from volume of tissue which delayed arrival of an injected tracer agent (time to maximum of the residue function [Tmax]) exceeding 6 secs)*



Volume of Ischemic Core, 23 ml
Ischemic core

Mismatch volume, 105 ml
Mismatch ratio, 5.6

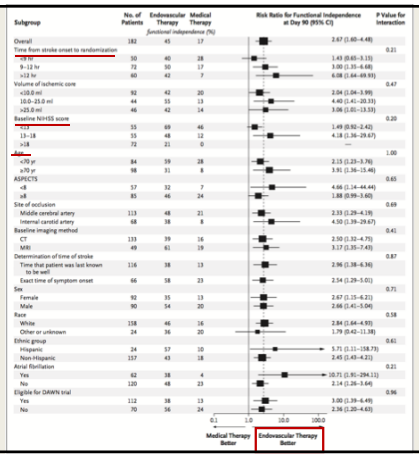
Volume of Perfusion Lesion, 128 ml
Perfusion delayed = penumbra

Table 1. Baseline Characteristics of the Patients and Features of Thrombectomy.*

Characteristic	Endovascular Therapy (N=92)	Medical Therapy (N=90)
Median age (IQR) — yr	70 (59–79)	71 (59–80)
Female sex — no. (%)	46 (50)	46 (51)
Median NIHSS score (IQR)†	16 (10–20)	16 (12–21)
Stroke onset witnessed — no. (%)		
Yes‡	31 (34)	35 (39)
No		
Symptoms were present on awakening	49 (53)	42 (47)
Symptoms began during wakefulness	12 (13)	13 (14)
Treatment with intravenous t-PA — no. (%)§	10 (11)	8 (9)
Imaging characteristics¶		
Qualifying imaging — no. (%)		
CT perfusion imaging	69 (75)	64 (71)
Diffusion and perfusion MRI	23 (25)	26 (29)
Median volume of ischemic core (IQR) — ml	9.4 (2.3–25.6)	10.1 (2.1–24.3)
Median volume of perfusion lesion (IQR) — ml‖	114.7 (79.3–146.3)	116.1 (73.4–158.2)
Occlusion site on baseline CTA or MRA — no. (%)		
Internal carotid artery	32 (35)	36 (40)
Middle cerebral artery**	60 (65)	54 (60)
Median ASPECTS on baseline CT (IQR)††	8 (7–9)	8 (7–9)
Process measures — hr:min		
Median time from stroke onset to qualifying imaging (IQR)	10:29 (8:09–11:40)	9:55 (7:59–12:20)
Median time from stroke onset to randomization (IQR)	10:53 (8:46–12:21)	10:44 (8:42–13:04)
Median time from qualifying imaging to femoral puncture (IQR)	0:59 (0:39–1:27)	NA
Median time from femoral puncture to reperfusion (IQR)	0:38 (0:26–0:59)	NA

Table 2. Clinical and Imaging Outcomes.

Outcome	Endovascular Therapy (N=92)*	Medical Therapy (N=90)	Odds Ratio or Risk Ratio (95% CI)††	P Value
Primary efficacy outcome: median score on modified Rankin scale at 90 days (IQR)‡	3 (1–4)	4 (3–6)	2.77 (1.63–4.70)§	<0.001
Secondary efficacy outcome: functional independence at 90 days — no. (%)¶	41 (45)	15 (17)	2.67 (1.60–4.48)	<0.001
Safety outcomes — no. (%)				
Death at 90 days	13 (14)	23 (26)	0.55 (0.30–1.02)	0.05
Symptomatic intracranial hemorrhage‖	6 (7)	4 (4)	1.47 (0.40–6.55)	0.75
Early neurologic deterioration	8 (9)	11 (12)	0.71 (0.30–1.69)	0.44
Parenchymal hematoma type 2	8 (9)	3 (3)	2.61 (0.73–14.69)	0.21
Imaging outcomes**				
Median infarct volume at 24 hr (IQR) — ml	35 (18–82)	41 (25–106)	—	0.19
Median infarct growth at 24 hr (IQR) — ml	23 (10–75)	33 (18–75)	—	0.08
Reperfusion >90% at 24 hr — no./total no. (%)	59/75 (79)	12/67 (18)	4.39 (2.60–7.43)	<0.001
Complete recanalization at 24 hr — no./total no. (%)	65/83 (78)	14/77 (18)	4.31 (2.65–7.01)	<0.001
TICI score of 2b or 3 — no./total no. (%)	69/91 (76)	—	—	



DEFUSE3 study

- Endovascular thrombectomy for AIS 6 - 16 hours plus standard medical therapy resulted in better functional outcomes than standard medical therapy alone among patients with proximal MCA/ICA occlusion and a region of tissue that was ischemic but not yet infarcted.

Mechanical thrombectomy

AHA/ASA Guideline

2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

Reviewed for evidence-based integrity and endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons

Endorsed by the Society for Academic Emergency Medicine

3.7. Mechanical Thrombectomy (Continued)	COR	LOE
7. In selected patients with AIS within 6 to 16 hours of last known normal who have LVO in the anterior circulation and meet other DAWN or DEFUSE 3 eligibility criteria, mechanical thrombectomy is recommended.	I	A
8. In selected patients with AIS within 6 to 24 hours of last known normal who have LVO in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy is reasonable.	IIa	B-R

Outline

- Thrombolytic therapy
- Mechanical Thrombectomy
- **Antiplatelet drug**
- Anticoagulant drug
- Other management

Antiplatelet drug

- Aspirin 300 - 325 mg/d within 48 hr
  - *Aspirin allergy consider other antiplatelets: cilostazol 200 mg/d*
- Double antiplatelets: clopidogrel 300 mg loading dose then clopidogrel 75 mg/d + baby aspirin 21 d may benefit for TIA with ABCD2 score ≥ 4 or ischemic stroke with NIHSS ≤ 3
- Case prior stroke with ASA consider other antiplatelet:
  - *clopidogrel75mg/d*
  - *cilostazol200mg/d*
  - *aspirin25 mg+ extended release dipyridamole 200 mg bid*

Other Antiplatelet drug for AIS ?

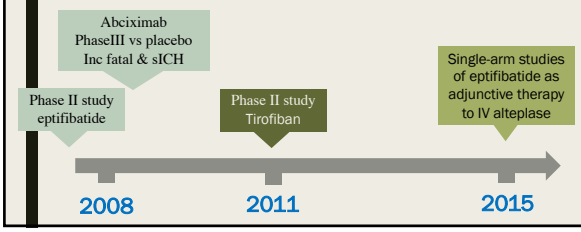
- Glycoprotein IIb/IIIa receptor antagonists
  - *Eptifibatide*
  - *Abciximab*
  - *Tirofiban*
- Ticagrelor

Glycoprotein IIb/IIIa receptor antagonists

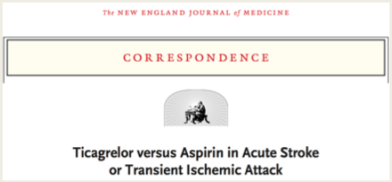
- A recent Cochrane review of IV glycoprotein IIb/IIIa receptor antagonists in the treatment of AIS found that these agents are associated with a significant risk of ICH without a measurable improvement in death or disability.

Cochrane Database Syst Rev. 2014:CD005208.

Further research is required



Ticagrelor



- SOCRATES a randomized, double-blind, placebo-controlled trial of ticagrelor vs aspirin
- AIS (minor stroke NIHSS <=5) or TIA (ABCD2>=4) Treated was begun within 24 hrs
- Primary outcome of time to the composite end point of stroke, myocardial infarction (MI), or death up to 90 days
- Ticagrelor was not found to be superior to aspirin (HR, 0.89; 95% CI, 0.78–1.01; *P*=0.07).

N Engl J Med. 2016;375:1395.

Antiplatelet drug

AHA/ASA Guideline

2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

Reviewed for evidence-based integrity and endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons

Endorsed by the Society for Academic Emergency Medicine

6. Ticagrelor is not recommended (over aspirin) in the acute treatment of patients with minor stroke.	III: No Benefit	B-R

SOCRATES

Ticagrelor vs ASA

THALES
(Ongoing study)
Ticagrelor+ASA vs ASA

Outline

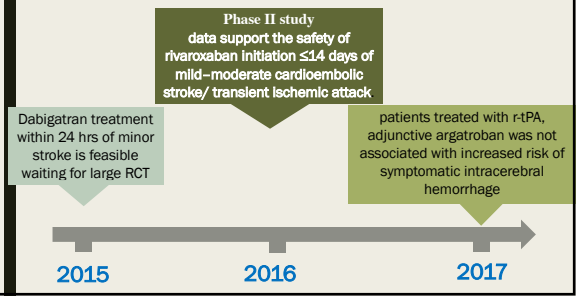
- Thrombolytic therapy
- Mechanical Thrombectomy
- Antiplatelet drug
- **Anticoagulant drug**
- Other management

Anticoagulant drug: NOACs

- Dabigatran
- Argatroban
- Rivaroxaban
- Apixaban
- Edoxaban

NOACs

- For acute ischemic stroke
- Further research is required



NOACs

- Several prospective observational studies and early-phase trials are ongoing
  - https://clinicaltrials.gov/ct2/show/study/NCT02279940
    Rivaroxaban Acute Stroke Safety Study (RASS)
  - https://clinicaltrials.gov/ct2/show/NCT02042534
    Rivaroxaban Versus Warfarin in Acute Ischemic Stroke With Atrial Fibrillation (TripleAXEL)
  - https://clinicaltrials.gov/ct2/show/NCT02283294
    Apixaban for Early Prevention of Recurrent Embolic Stroke and Hemorrhagic Transformation (AREST)

Outline

- Thrombolytic therapy
- Mechanical Thrombectomy
- Antiplatelet drug
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- **Other management**

Other management

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3.12. Neuroprotective Agents	COR	LOE
1. At present, no pharmacological or non-pharmacological treatments with putative neuroprotective actions have demonstrated efficacy in improving outcomes after ischemic stroke, and therefore, other neuroprotective agents are not recommended.	III: No Benefit	A
4.4. Temperature	**COR**	**LOE**
2. The benefit of induced hypothermia for treating patients with ischemic stroke is not well established. Hypothermia should be offered only in the context of ongoing clinical trials.	IIb	B-R

Summary

- Thrombolytic therapy
  - Desmoteplase, Teneteplase
- Mechanical Thrombectomy
  - DAWN, DEFUSE3
- Antiplatelet drug
  - Glycoprotein IIb/IIIa, Ticagrelor
- Anticoagulant drug
  - NOACs
- Other management
  - Neuroprotective, hypothermia

THANK YOU FOR YOUR ATTENTION

North-Eastern Stroke Research Group