

**tPA Use in ED Stroke Patients:
 What the Data Tells Us About Current Use**

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Disclosures

- AstraZeneca, advisory board
- Genentech, speakers bureau

- ACEP Scientific Review Committee
- Executive Board, Foundation for Education and Research in Neurologic Emergencies

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NINDS Trial Results
 Percentage with favorable outcome

	t-PA	Placebo
No. of patients: 312	157	145
Modified Rankin Scale	40%	28%
Glasgow Outcome Scale	43%	32%
NIHSS	34%	20%
Symptomatic ICH (within 36 hr)	6.4%	0.6%
Death (by 90 days)	17%	21%

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IV Thrombolysis

- 14% absolute increase for the best clinical outcomes as measured by an NIHSS of 0-1.
- Benefit = Need to treat 8 patients with t-PA in order to have one additional patient with this best outcome.
- 6% absolute increase in the number of symptomatic ICH.
- Harm = Will have one symptomatic ICH for every 16 patients treated with t-PA.
- 2 patients will have a minimal or no deficit for everyone patient with a symptomatic ICH

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Phase IV t-PA trials

Author	Eligible patients	Patients receiving tPA(%)	Mean time to Rx	Median NIHSS score	Favorable outcome	% ICH	% Symptomatic ICH	% Protocol deviation
NINDS		312		14	31-54%	10.9%	6.4%	
Chiu	1035	30(2.9%)	2'37"	14	63%	10%	6.6%	
Tanne		189	>2'	11-15		9%	5.8%	30%
Wang	900	57(6.3%)	2'28"	15	44-54%	9%	5%	9%
Buchan	1540	68(4.4%)		15	95%	31%	9%	16%
Albers		389	2'44"	13	35-43%	11.5%	3.3%	33%
Katzan	3948	70(1.8%)		12		22%	15.7%	50%
Chapman	2556	46(1.8%)	2'45"	14	30-48%	9%	2.2%	17%
Grotta	1689	269(16%)	2'17"	14	33%		4.5%	13%
Bravata		63		15		17%	6%	67%
Total	12,282	928(5.8%)	2'25"	10-15	33-95%	9.6%	5.2%	13-67%

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Meta-analyses

- Wardlaw et al.
- Net benefit despite hazards
- For 1000 treated up to 6hrs, 55 improve, 20 die
- Heterogeneity and wide CI make results unreliable
- Additional trial data required

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Meta-analyses

- Graham et al., 15 published reports
- ICH rate 5.2%, total death rate 13.4%
- All better than NINDS
- Lysis can be used safely across wide variety of practice settings

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Re-analysis

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NINDS ICH Analysis

Risk Factors for ICH:

- Baseline NIHSS > 20
- Age > 70 years
- Ischemic changes present on initial CT
- Glucose > 300 mg/dl (16.7 mmol/L)

# of Risk Factors	# of patients treated with t-PA (n=310)	# Symptomatic ICHs (# of placebo patients with ICH)	Percentage (%)
0	114	2 (1)	1.8
1	144	7 (1)	4.9
> 1	52	11	21.2

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Re-analysis Conclusions

- The independent reanalysis of the NINDS t-PA clinical trial confirms the results from the initial *NEJM* publication
- Support the use of t-PA in stroke patients within three hours of symptom onset
- Number needed to treat calculation based on this reanalysis confirms that approximately 8-10 patients need to be treated with t-PA in order to cause one extra patient to have the best clinical outcome.
- 2 patients will improve for every one that develops a symptomatic ICH

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Conclusions

- Data supports the use of IV t-PA when the NINDS protocol is strictly followed
- Develop a protocol that allows patients to have the greatest chance of receiving therapy as quickly as possible
- Sooner may be better, more work to be done on subgroups
- Document well on all patients, t-PA or not

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Questions?

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