CNY RSTAC
REGIONAL STROKE ADVISORY COUNCIL

Agenda Items- March 18th, 2022 10:00 am

- Call to Order
- Approval of Previous Meeting Minutes
- Chairman Update
  - International Stroke Conference 2022 Highlights
- Old Business
- New Business
  - Discussion- Tenecteplase regional roll-out
  - FAST-ED Training Video and handout
  - Officer nominations (Chair, Vice-chair, Secretary)
- New York State Updates
  - New Stroke Centers / Designation update
  - New York State Stroke Advisory Committee Updates
- Educational Opportunities
  - Upstate – Virtual RUSH Presentation series
  - North Country EMS Spring Fling
- Regional Reports/ Round table
- Adjournment

UPSTATE
COMPREHENSIVE STROKE CENTER

UPSTATE MEDICAL UNIVERSITY
DEPARTMENT OF NEUROLOGY
Cerebrovascular and Neurocritical Care Division

Highlights from ISC 2022

Julius Gene Latorre, MD, MPH, FAAN, FAHA, FNCS, FCCM
Professor of Neurology and Neurosurgery
Upstate Medical University
Division of Vascular and Neurocritical Care

What's New: IVT plus EVT

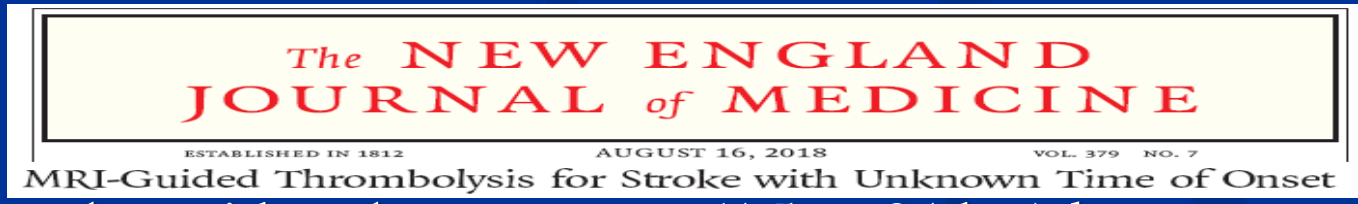
- More stroke centers switching to TNK
- Multiple trials on TNK beyond 4.5hrs
- TNK appears safe(r) vs Alteplase

IVT Beyond 4.5 hours

EXTEND

- Identify moderate stroke not EVT-eligible with salvageable tissue using advanced imaging (e.g. core <70cc, mismatch >1.2) at 4.5 to 9 hrs from LKW
- Excludes lacunar infarct

WAKE UP



- Identify strokes with unknown onset (4.5 to 24 hrs) but potentially early per imaging (DWI+ without FLAIR)
- Hard to get MRI quickly in emergency situation

Ma et al. NEJM 2019;380:1795-1803
Thomalla et al. NEJM 2018;379:611-622

IVT in px undergoing EVT

- ISSUES – possible ADVANTAGE of bridging therapy
  - IVT plus EVT
    - Can increase recanalization before EVT
    - Can reduce time to recanalization
    - Can ensure patient receive acute treatment (in event EVT can't be performed due to patient anatomy, EVT process delay, etc)

IVT in px undergoing EVT

- ISSUES – possible DISADVANTAGE of bridging therapy
  - IVT plus EVT
    - Can increase symptomatic hemorrhage (sICH)
    - Can increase mortality (due to sICH)
    - Can reduce good outcome due to potential neurotoxicity of alteplase
    - Can add cost to care of patients

EVT vs IVT+EVT

	DIRECT-MT	DEVT	SKIP (used 0.6mg/kg)	MR CLEAN NOIV	SWIFT-DIRECT
Year	2020	2021	2021	2021	2022?
Country	China	China	Japan	Europe	Europe-Can
Design	RCT-open	RCT-open	RCT-open	RCT-open	RCT-open
N	656	234	204	539	404
NIHSS	17 vs 17	16 vs 16	19 vs 17	16 vs 16	n/a
sICH	4.3 vs 6.1	6.1 vs 6.8	5.9 vs 7.7	5.9 vs 5.3	1.5 vs 4.9
Mortality	17.7 vs 18.8	17.2 vs 17.8	7.9 vs 8.7	20.5 vs 15.8	n/a
mRS 0-2 at 90d	36.4 vs 36.8	54.3 vs 46.6	59.4 vs 57.3	49.1 vs 51.1	57 vs 65
EVT non-inferior	YES	YES	NO	NO	NO

EVT vs IVT+EVT

- Evidence showing mixed results re non-inferiority
- All studies involve open label use (can introduce bias)
- No increase in sICH, no increase in mortality
- General conclusion: EVT alone
  - Not superior to IVT+EVT
  - Can not be recommended for routine practice
  - Ongoing trial - DIRECT-SAFE
  - Possible potential use in selected patients

IVT plus, ongoing trial

- MOST Phase III RCT Double blind trial
  - IVT plus IV antithrombotics
    - ARM 1 – Eptifibatide (GIIb/IIIa inhibitor) 135ug/kg bolus +75ug/kg/min x 2 hours
    - ARM 2 - Argatroban (Direct Thrombin inhibitor) 100ug/kg bolus + 3ug/kg/min x 12 hours
    - ARM 3 - placebo
  - AIS with LKW <3hrs and NIHSS 6 + with or without LVO
  - USA
  - Target N=1200 (292 randomized as of 8 Feb 2022)

Adapted from ISC 2022 presentations by Opeolu Adeoye MD Feb 10, 2022

IVT plus, ongoing trial

- DUMAS trial Phase 2 single blind randomized
  - Dual thrombolytic
    - ARM 1: mutant Pro-urokinase plus low dose IVT (Alteplase 5mg IV bolus plus Hispro-UK 40mg/hr x 60 min)
    - ARM 2: IVT standard of care
  - Ischemic stroke with NIHSS 1+, LKW within 4.5 hours, NOT candidate for EVT
  - Netherlands
  - Target N = 200 (134 randomized) Estimated completion date July 2022

Adapted from ISC 2022 presentations by Prof Diederik Dippel Feb 10, 2022

IVT plus, ongoing trial

- ACTISAVE trial Phase 2/3 RCT double blind
  - IVT plus Glenzocimab (ACT017) anti-GP VI
  - IVT plus IV antithrombotics
    - ARM 1 – IVT plus Glenzocimab (aAnti GP VI) 1000mg IV
    - ARM 2 - IVT plus placebo
  - AIS with LKW <4.5 hrs and NIHSS 4 + with or without LVO
  - Europe/North America
  - Target N=1000 Estimated completion Dec 2025

Promising Novel agents

- ADAMTS13 (cleaves vWF) -preclinical
- DTR-031 (vWF antagonist) - preclinical
- LT3001 (lytic and neuroprotectant) – clinical
- TS23 (alpha-2 antiplasmin inhibitor) – clinical
- RNS60 (neuroprotectant) – clinical trial
- DM199 (tissue kallikrein) – clinical trial
- 3K3A-APC (activated Protein C) – clinical trial
- NA-1 (neuroprotectant) – clinical trial

Summary 1

- IVT
  - Remains gold standard for LKW 0-4.5hrs
  - TNK data promising, maybe safe(r)
  - More and more centers switching to TNK (simpler, safer dosing, cheaper)
  - Reduces mortality in severe strokes (NIHSS >18)

Summary 2

- IVT-mediated thrombolysis may be improved by combination therapy
  - Within 3 hours time window
    - IVT plus eptifibatide or argatroban (MOST)
  - Within 4.5 hrs time window
    - IVT plus 3K3A-APC (RHAPSODY)
    - IVT plus glenzocimab (ACTIMIS)
    - IVT plus mutant pro-urokinase (DUMAS)

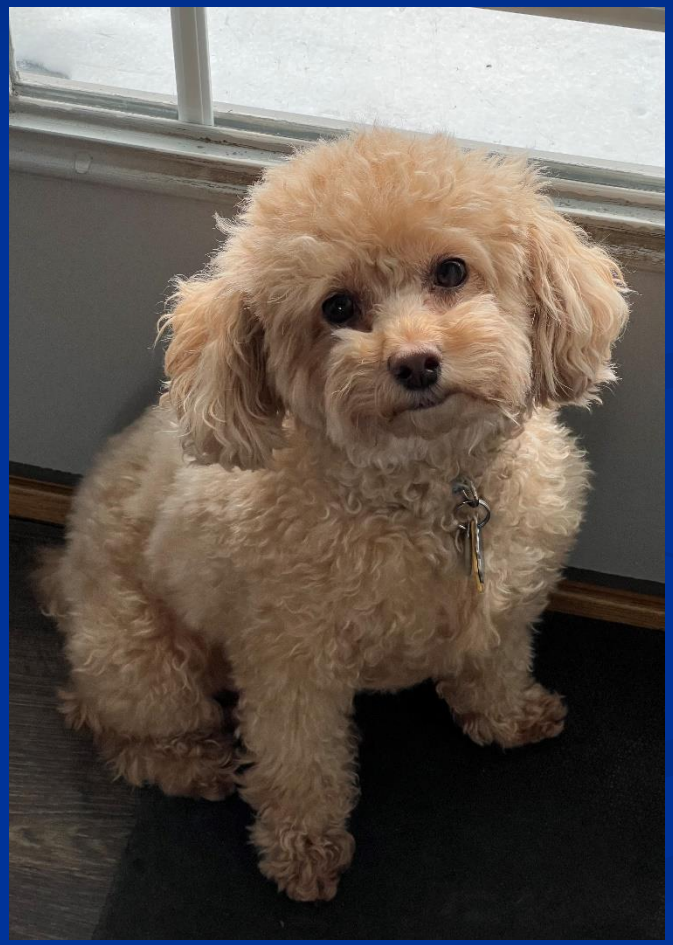
Summary 3

- Promising neuroprotective agents
  - With LVO
    - RNS60
    - PP-007 Sanguinate
    - Nerinetide (NA-1)
  - No LVO
    - KLK1

Summary 4

- Promising IVT alternatives focusing on novel therapeutic targets
  - Targeting vWF
    - ADAMS13
    - DTR-031
  - Combination lytic and neuroprotectant
    - LT3001
  - alpha2 Antiplasmin inhibitor
    - TS23

Thank YOU!



Tenecteplase Update

- Regional roll-out going well
  - Mercy (Catholic Health System) and Samaritan Medical Center are live
  - MVHS, Crouse, Rochester General, and Arnot Health looking to go live May 2022
- We will continue education and endorsing this thrombolytic switch
  - Tenecteplase Starter Kit
  - Additional education to EMS?

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Tenecteplase Update

INTERNATIONAL STROKE CONFERENCE 2022 ORAL ABSTRACTS

SESSION TITLE: ACUTE NONENDOVASCULAR TREATMENT ORAL ABSTRACTS I

Abstract 43: Comparative Effectiveness Of Routine Tenecteplase Thrombolysis In Acute Stroke Compared With Alteplase: An INternational Collaboration (CERTAIN Collaboration): Rates Of Symptomatic Intracranial Hemorrhage

Steven J Warach, Anna Ranta, Shlee S Song, Daniel Gibson, Adam Wallace, James Beharry, Christopher Bladin, Timothy J Kleinig, Jackson Harvey, Vinodh T Doss, Ruth Marescalco, John N Fink, ... See all authors

- Abstract presented at 2022 International Stroke Conference
- Registry study including 7,891 patients given IV TNK or ALT for AIS
- TNK had lower symptomatic ICH rates (ALT 3.71% vs. TNK 2.13%, p = 0.002)
- TNK had lower symptomatic ICH rates in non-thrombectomy patients
- TNK did not have lower symptomatic ICH rates in thrombectomy patients

TNK appears at least as safe versus ALT in AIS, and it may potentially have a safety benefit

Warach SJ, et al. Stroke 2022; 53: A43.

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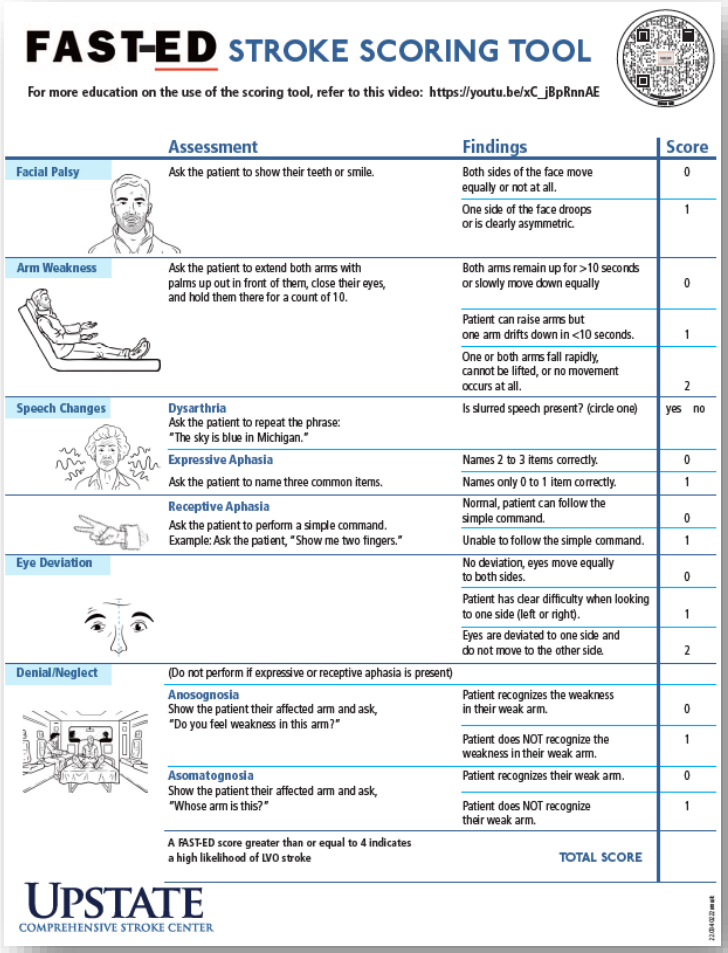
FAST-ED Update



FAST-ED STROKE SCORING TOOL

For more education on the use of the scoring tool, refer to this video: https://youtu.be/xC_jBpRnnAE

	Assessment	Findings	Score
Facial Palsy	Ask the patient to show their teeth or smile.	Both sides of the face move equally or not at all.	0
		One side of the face droops or is clearly asymmetric.	1
Arm Weakness	Ask the patient to extend both arms with palms up out in front of them, close their eyes, and hold them there for a count of 10.	Both arms remain up for >10 seconds or slowly move down equally	0
		Patient can raise arms but one arm drifts down in <10 seconds.	1
		One or both arms fall rapidly, cannot be lifted, or no movement occurs at all.	2
Speech Changes	**Dysarthria** Ask the patient to repeat the phrase: "The sky is blue in Michigan."	Is slurred speech present? (circle one)	yes no
	Expressive Aphasia Ask the patient to name three common items.	Names 2 to 3 items correctly.	0
		Names only 0 to 1 item correctly.	1
	Receptive Aphasia Ask the patient to perform a simple command. Example: Ask the patient, "Show me two fingers."	Normal, patient can follow the simple command.	0
		Unable to follow the simple command.	1
Eye Deviation		No deviation, eyes move equally to both sides.	0
		Patient has clear difficulty when looking to one side (left or right).	1
		Eyes are deviated to one side and do not move to the other side.	2
Denial/Neglect	(Do not perform if expressive or receptive aphasia is present)		
	Anosognosia Show the patient their affected arm and ask, "Do you feel weakness in this arm?"	Patient recognizes the weakness in their weak arm.	0
		Patient does NOT recognize the weakness in their weak arm.	1
	Asomatognosia Show the patient their affected arm and ask, "Whose arm is this?"	Patient recognizes their weak arm.	0
		Patient does NOT recognize their weak arm.	1
	A FAST-ED score greater than or equal to 4 indicates a high likelihood of LVO stroke	TOTAL SCORE	

UPSTATE COMPREHENSIVE STROKE CENTER

- Small workgroup continues to look at FAST-ED Education
- Second training video created at regional request
  - Video teaches scoring of FAST-ED using a new tool
  - Tool collaborated with MVHS team for similar messaging across regions
  - Video available FASTED Series 2 Stroke Scoring Tool - YouTube
- North Country EMS Spring Fling advertisement
- AHA Grant funding available for completion of training

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Officer Nominations

OFFICERS (from 2021 By-laws)

- The Chair of the council shall be a stroke medical director of a Comprehensive Stroke Center The Vice-Chair of the council shall be a stroke medical director from a Comprehensive Stroke Center (CSC) or Primary Stroke Center (PSC) center within the region.
- (CSC) or Primary Stroke Center (PSC) within the region.
- The Secretary of the council shall be a Stroke Program Manager/Stroke Coordinator Comprehensive Stroke Center (CSC) or Primary Stroke Center (PSC) center within the region.

TERM OF OFFICE

- The Chair will serve a two-year term.
- The Vice-chair will serve a two-year term. The Vice-chair will assume the Chair's role if the Chair is unable to complete the full term.
- The Secretary will serve a two-year term.
- If the role of the vice-chair or secretary becomes vacant, the Chair may appoint a member from the council to fill the role for the duration of the remaining term.
- There is no term limit for any officer position.

OFFICER ELECTION

- Nominations will be requested **before or during the March meeting**. A slate of officers is to be presented at this meeting.
- A **virtual survey** of officers will be sent to the council before the June meeting for anonymous voting. Officers will be elected by the majority of those voting. In the event of a tie, an additional virtual survey of the top two candidates will be sent to the council for voting. The officer will be elected by the majority of those voting.
- **New officers will be announced during the June meeting**. The term shall take effect following the June meeting.

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New York State Updates

- Coverdell Updates
  - Strategy areas: Track and monitor clinical measures, Implement a team-based approach, link community resources, and clinical services.
  - Priority Regions: Tasked from CDC to work in priority regions to improve handoffs and communication with EMS and hospitals, reviewing data on stroke hospitalizations and mortality by county, identifying high burdens of stroke, engaging the partners in identified regions to increase collaborations.

- NYS DOH
  - HERDS Survey opened May 9th
  - Designation deadline extended until March 2023
  - Some accrediting bodies may be experiencing accreditation scheduling delays
  - NYS Stroke Guidance document currently in revision
    - Stroke Education requirements being looked at
  - Reach out to Josh with any problems or concerns

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