Large Core Stroke Trials

THE UNIVERSITY OF KANSAS HEALTH SYSTEM

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Disclosures

Consultant – Stryker Neurovascular

Consultant – Q'Apel

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Outline

EVT stroke trials

Large core stroke trials

EVT Cases

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Stroke Trial	mTICI 2B/3	90 day mRS ≤2 EVT	90 day mRS ≤2 SC
IMS 3 (2013)	23-44%	40.8%	48.7%
MR RESCUE (2013)	25%	12%	11%
SYNTHESIS-EXPANSION (2013)	Not reported	30.4%	34.8%
MR CLEAN (2015)	58.7%	32.6%	19.1%
SWIFT PRIME (2015)	88%	60%	35.5%
ESCAPE (2015)	72.4%	53%	29.3%
EXTEND-IA (2015)	86%	71%	40%
REVASCAT (2015)	66%	43.7%	28.2%
DAWN (2018)	84%	48.6%	13.1%
DEFUSE-3 (2018)	76%	44.6%	16.7%

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Stroke

3.7.3. 6 to 24 Hours From Onset	COR	LOE	New, Revised, or Unchanged
1. 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	New recommendation.
2. In selected patients with AIS within 16 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	New recommendation.
The DAWN trial used clinical-core mismatch (a combination of NIHSS score and imaging findings on CTP or DW-MRI) as eligibility criteria to select patients with large anterior circulation vessel occlusion for treatment with mechanical thrombectomy between 6 and 24 hours from last known normal. This trial demonstrated an overall benefit in function outcome at 90 days in the treatment group (mRS score 0–2, 49% versus 13%; adjusted difference, 33% [95% CI, 21–44]; posterior probability of superiority >0.999).[9] In DAWN, there were few strokes with witnessed onset (12%). The DEFUSE 3 trial used perfusion-core mismatch and maximum core size as imaging criteria to select patients with large anterior circulation occlusion 6 to 16 hours from last seen well for mechanical thrombectomy. This trial showed a benefit in functional outcome at 90 days in the treated group (mRS score 0–2, 44.6% versus 16.7%; RR, 2.67 [95% CI, 1.60–4.48]; P<0.0001).[10] Benefit was independently demonstrated for the subgroup of patients who met DAWN eligibility criteria and for the subgroup who did not. DAWN and DEFUSE 3 are the only RCTs showing benefit of mechanical thrombectomy >6 hours from onset. Therefore, only the eligibility criteria from one or the other of these trials should be used for patient selection. Although future RCTs may demonstrate that additional eligibility criteria can be used to select patients who benefit from mechanical thrombectomy, at this time, the DAWN or DEFUSE 3 eligibility should be strictly adhered to in clinical practice.[11,12]			See Table XVII in online Data Supplement 1.

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DEFUSE 3

NIHSS ≥6

prestroke mRS 0-2

initial infarct volume (ischemic core) <70 mL

ratio of volume of ischemic tissue (penumbra) to infarction of ≥1.8

absolute volume of potentially reversible ischemia of ≥15 mL

DAWN

NIHSS ≥10

prestroke mRS 0-1

core-clinical mismatch on MRI-DWI or CTP

- **0-20 mL core, NIHSS ≥10, and ≥80 years**
- **0-30 mL core, NIHSS ≥10, and <80 years**
- **31-50 mL core, NIHSS ≥20 and, <80 years**

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Why?


Ischemic stroke

Original research

Endovascular thrombectomy in patients with large core ischemic stroke: a cost-effectiveness analysis from the SELECT study

Amrou Sarraj, Elena Pizzo, Kyriakos Lobotesis, James C Grotta, Ameer E Hassan, Michael G Abraham, Spiros Blackburn, Arthur L Day, Mark J Dannenbaum, William Hicks, Nirav A Vora, Ronald F Budzik, Anjail Z Sharrief, Sheryl Martin-Schild, Clark W Sitton, Deep Kirithikar Pujara, Maarten G Lansberg, Rishi Gupta, Gregory W Albers, Wolfgang G Kunz, on behalf of the SELECT Investigators

Large core = bad outcomes?

SELECT trial - 361 patients

105 large core on CT or CTP (EVT 62, MM 43)

19 (31%) EVT vs 6 (14%) MM patients achieved mRS 0–2 (OR 3.27, 95%CI 1.11 to 9.62, P=0.03) with a shift towards better mRS (95%CI 1.05 to 4.31, P=0.04)

projected lifetime of patients with large core, EVT --> incremental costs of $33,094 and a **gain of 1.34 quality-adjusted life years** (QALYs) per patient

HERMES, DAWN, DEFUSE 3 trials --> **gain of 1.62, 2.36 and 2.21 QALYs**, respectively

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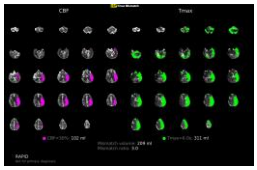
Small Core vs Large Core EVT

Small Core
- Bad → good

Large Core
- Bad → better →/? Good
- Ambulate?

Avoid herniation → hemicraniectomy?



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RESCUE-Japan LIMIT


The NEW ENGLAND JOURNAL of MEDICINE

Endovascular Therapy for Acute Stroke with a Large Ischemic Region

MRI ASPECTS 3-5

1:1 ratio to EVT with MM or MM alone within 6 hours after LKN or within 24 hours if no early change on MRI-DWI

Alteplase (0.6 mg per kilogram) used when appropriate in both groups

Primary outcome mRS 0-3 at 90 days

Secondary outcomes → shift across the range of mRS scores toward a better outcome at 90 days and an improvement of ≥8 points in the NIHSS score (0-42) at 48 hours

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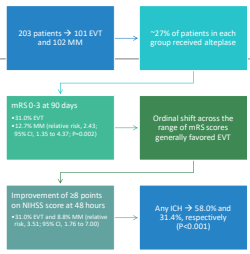
Results



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ANGELS-ASPECT

Multicenter, prospective, open-label, randomized trial in China

Anterior circulation LVO and ASPECTS 3-5 or core volume of 70-100 ml

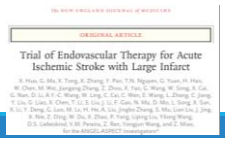
1:1 ratio within 24 hours to EVT and MM or MM alone

Primary outcome → mRS at 90 days

Primary objective → determine whether a shift in distribution of mRS at 90 days

Secondary outcomes → mRS 0-2 and 0-3

Primary safety outcome → sICH within 48 hours


ORIGINAL ARTICLE

Trial of Endovascular Therapy for Acute Ischemic Stroke with Large Infarct

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Results

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SELECT 2

- Prospective, randomized, open-label, adaptive, international trial → LVO of ICA or first segment of MCA → EVT vs MM within 24 hours
- ASPECTS 3-5 and/or core volume of ≥50 ml on CTP or MRI-DWI
- 1:1 ratio to EVT plus MM or MM alone
- Primary outcome → mRS at 90
- Secondary outcome → Functional independence

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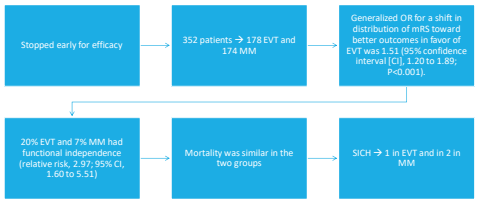
Results



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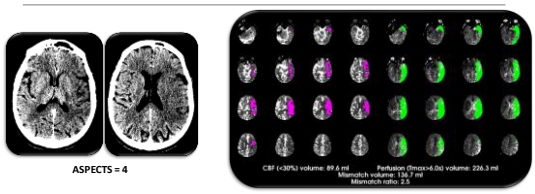
Unfavorable CT / Unfavorable CTP - Eligible



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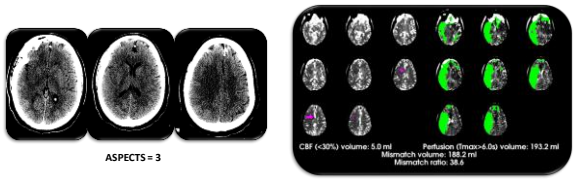
Unfavorable CT / Favorable CTP - Eligible



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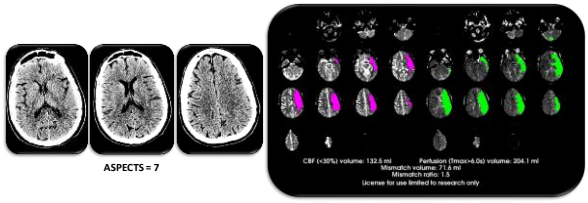
Favorable CT / Unfavorable CTP - Eligible



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Key Baseline Characteristics

		Medical Care Only (N=174)	Endovascular Thrombectomy Plus Medical Care (N=178)
Age (years), median (IQR)		67 (58-75)	66 (58-75)
Female Sex, n (%)		74 (42.5%)	71 (39.9%)
Right Hemisphere affected, n (%)		98 (56.3%)	98 (55.1%)
Occlusion location, n (%)	ICA	66 (37.9%)	80 (44.9%)
	MCA M1	100 (57.5%)	91 (51.1%)
	MCA M2	8 (4.6%)	7 (3.9%)
IV Thrombolysis, n (%)	Total	30 (17.3%)	37 (20.8%)
NIH Stroke Scale at Presentation to EVT Center		*19 (15-22)*	*19 (15-23)*
Time from Last Known Well to Randomization (minutes)		587.5 (349-919)	544.5 (316-920)
	0-6 hours	*45 (25.9%)*	*55 (30.9%)*
	6-24 hours	*129 (64.1%)*	*123 (69.1%)*
	0-12 hours	*110 (63.2%)*	*101 (58.0%)*
	12-24 hours	*68 (38.2%)*	*73 (42.0%)*
ASPECTS on Baseline CT		4 (4-5)	4 (3-5)
Imaging Modality Used to Estimate Ischemic Core, n (%)	CT Perfusion	169 (97.1%)	174 (98.3%)
	MR Diffusion	5 (2.9%)	3 (1.7%)
Estimated Ischemic core volume (ml)	Overall	*73 (52-111)*	*81.5 (57-118)*
	CT Perfusion	*70 (50-111)*	*81.5 (59-120)*
	MR Diffusion	*80 (34-104)*	*47 (16-49)*
Critically hypoperfused (Tmax >6s) lesion volume (ml)		169 (127-216)	171 (127-226)
Tissue Volume with Tmax >10s (ml)		111 (67-147)	107 (70.5-152.5)

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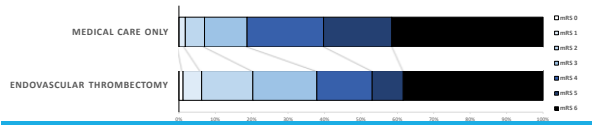
Primary Outcome – Intention-to-Treat Population

WMW measure of Superiority: 0.60, 95% CI: 0-55-0.65 --> **60% chance that a patient will have a better outcome**
GenOR: 1.51, 95% CI: 1.20-1.89 ***p=0.0004***

Number Needed to Treat: 4.94



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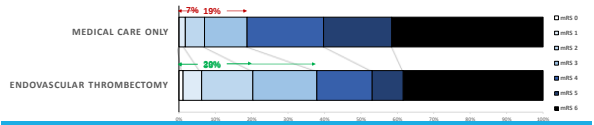
Key Secondary Outcomes – Intention-to-Treat Population

mRS 0-2: EVT: 20% vs MM: 7%, RR: 2.97, 95% CI: 1.60-5.51
NNT: 7.34
mRS 0-3: EVT: 38% vs MM: 19%, RR: 2.06, 95% CI: 1.43-2.96
NNT: 5.11



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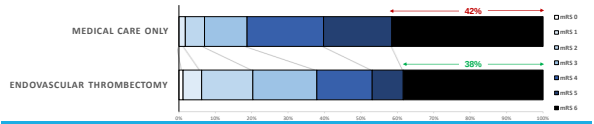
Safety Outcomes – Intention-to-Treat Population

Symptomatic ICH: EVT: 0.6% vs MM: 1.1%, ***RR: 0.49, 95% CI: 0.04-5.36***
Mortality: EVT: 38% vs MM: 42%, ***RR: 0.91, 95% CI: 0.71-1.18***
Early Neurological Worsening: EVT: 25% vs MM: 16%, RR: 1.59, 95% CI: 1.03-2.45



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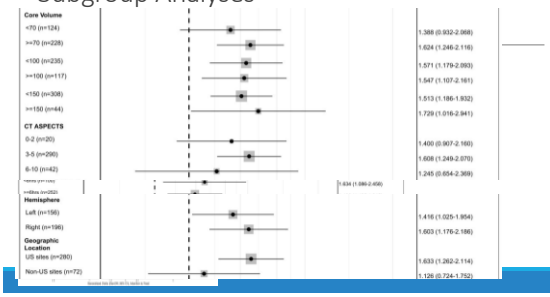
Subgroup Analyses



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Ischemic Core Subgroups

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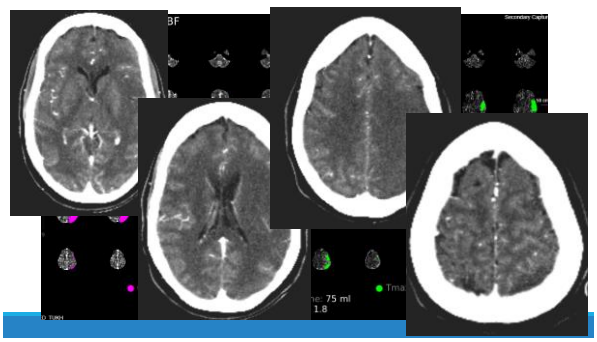

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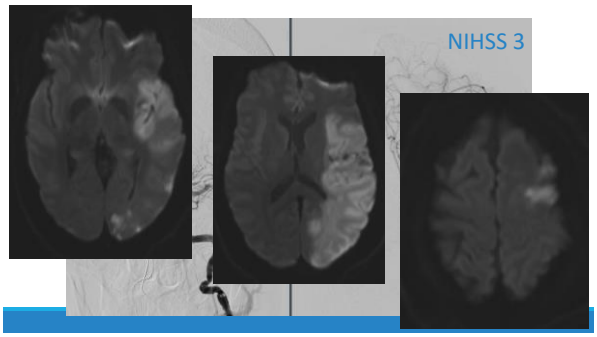

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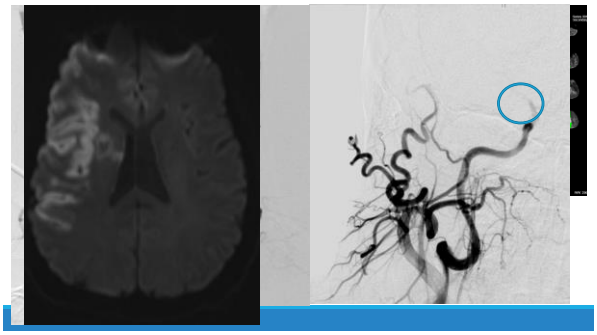

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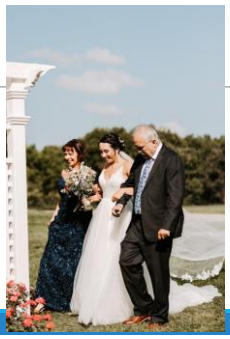
More than statistics, MRI scans, or CT scans...



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Future Directions

Direct to angio-suite

>24 hours

Sub-analyses from SELECT 2

Meta-analysis from large core trials (MAGNA)

Posterior circulation stroke

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Thank you.

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