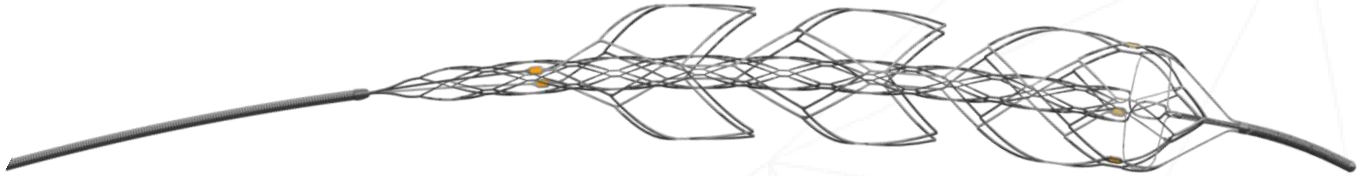
ARISE II Clinical Trial Primary Results

ARISE II

The Analysis of Revascularization in Ischemic Stroke With EmboTrap (ARISE II Trial)



Zaidat O, Bozorgchami H , Ribó M, Saver J, Mattle H, Chapot R, Narata A, Francois O, Jadhav A, Grossberg J, Riedel C, Tomasello A, Clark W, Nordmeyer H, Lin E, Nogueira R, Yoo A, Jovin T, Siddiqui A, Bernard T, Claffey M, ***Andersson T.***

On behalf of the ARISE II investigators

International Stroke Conference February 25, 2018

Disclosures

ARISE II

- Consultant for Neuravi, now Cerenovus

Background

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- Newer generation mechanical thrombectomy devices significantly improved outcomes in acute ischemic stroke therapy.
- However limitation to current technology exists:
  - Failure to achieve successful reperfusion (mTICI≥2b) in ~ 1/3 of the patients (In the Seers and Hermes RCT pooled analysis; the reperfusion rate reported at 71%).
  - Limited rate of Final near complete or complete (TICI 2c-3) reperfusion, with reported rates of up to 50%
  - Furthermore, First Pass/Attempt near complete or complete reperfusion was reported at still low rates of up to 30% (self and core lab reported)

•Goyal M, Menon BK, van Zwam WH, Dippel DW, MitchellPJ, Demchuk AM, et al. HERMES collaborators. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. Lancet. 2016 Apr 23;387(10029):1723-31.

•Campbell BC, Hill MD, Rubiera M, Menon BK, Demchuk A, Donnan GA, et al. Safety and Efficacy of Solitaire Stent Thrombectomy: Individual Patient Data Meta-Analysis of Randomized Trials. Stroke. 2016;47:798-806.

•Zaidat OO, Castonguay AC, Gupta R, Sun CJ, Martin C, Holloway WE, et al. The first pass effect: a new measure for stroke thrombectomy devices. (In Press), Accepted, *Stroke,* 2018

Background: EmboTrap Device

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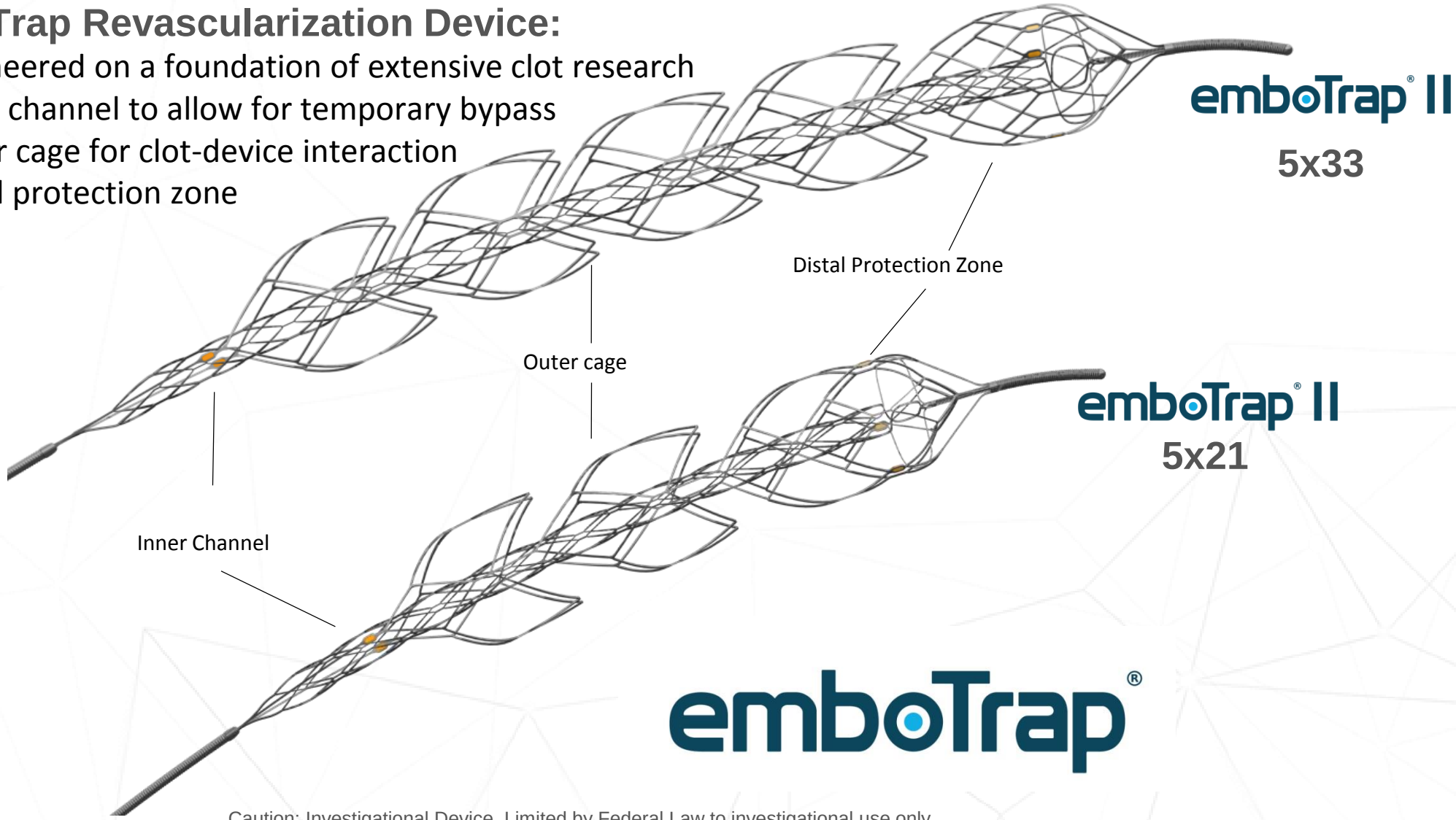
- **EmboTrap Revascularization Device:**
  - Engineered on a foundation of extensive clot research
  - Inner channel to allow for temporary bypass
  - Outer cage for clot-device interaction
  - Distal protection zone



ARISE II Team

ARISE II

Participating Sites:

- 19 Sites: 11 US sites, 8 European sites

Executive Committee

- Osama Zaidat, MD (Study PI)
- Tommy Andersson, MD (Study PI)
- Heinrich Mattle, MD
- Jeffrey Saver, MD
- Mairsil Claffey – Sponsor Representative

Steering Committee

- Hormozd Bozorgchami, MD
- Marc Ribo, MD
- Adnan Siddiqui, MD
- Ashutosh Jadhav, MD
- Ana Paula Narata, MD
- Albert Yoo, MD
- Rene Chapot, MD
- Jonathan Grossberg, MD

DSMB

- Steven Hetts, MD Chair
- Werner Hacke, MD
- Lotfi Hacein-Bey, MD
- Brijesh Mehta, MD
- Anthony Kim , MD
- Alex Abou-Chebl, MD
- Peter Shabe (Biostatistician)

CEC

- Steven Hetts, MD, Chair
- Lotfi Hacein-Bey, MD
- Anthony Kim, MD
- Alex Abou-Chebl MD

Core Lab

- Albert Yoo,MD Core Lab Director
- Intrinsic Imaging LLC (Massachusetts)

Sponsor

- Neuravi, now Cerenovus

Study Objectives

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Primary objectives:

- Assess the revascularization and safety outcomes of the EmboTrap device in acute ischemic stroke

Secondary objectives:

- Functional clinical outcomes at 90 days post treatment

Methods

ARISE II

- Study Design:
  - Open label, single arm, multi-center, prospective clinical study
  - Independent imaging core lab
  - Independent clinical event committee and DSMB
- Designed to secure 510(k) clearance of the EmboTrap® Revascularization Device
- Population: Anterior and Posterior Circulation LVO presenting with acute ischemic stroke
- Sample Size: Based on pre-specified performance goal from TREVO2, and SWIFT trials result. With an assumption of independently adjudicated revascularization success with EmboTrap is 68%; 176 patients would provide 90% power and 0.025 significance level.
- Final Sample Size 228, to allow for 30% Attrition rate

Method: ARISE II Study Endpoints

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Primary Efficacy Endpoint	• **mTICI 2b-3** within 3 passes of the EmboTrap device without rescue (*inclusive of 2c rating) (core-lab adjudicated)*
Primary Safety Endpoint	• Composite of occurrence of symptomatic intra-cerebral hemorrhage (**sICH**) within 24 hours post-procedure, together with other serious adverse device events *(CEC adjudicated)*
Secondary Endpoints	• modified Rankin Score (**mRS) ≤2** at 90 days • Procedure and time to treat • Mortality rate (Procedure-related at 7d, all-cause at 90d) • SADE (serious adverse device events) • Neurological deterioration by ≥4 points on NIHSS at 24 hrs

Method: Angiographic outcome measure

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- The revascularization grading was performed using mTICI scale
- The independent core lab adjudicated the angiograms after:
  - Each Device Pass/Attempt providing independent adjudication of First Pass Effect
  - Three Passes (the primary study endpoint)
  - At the end of the procedure
- Use of a different device prior to 3 passes was considered failure
- Use of Aspiration Pump with any device pass was considered failure

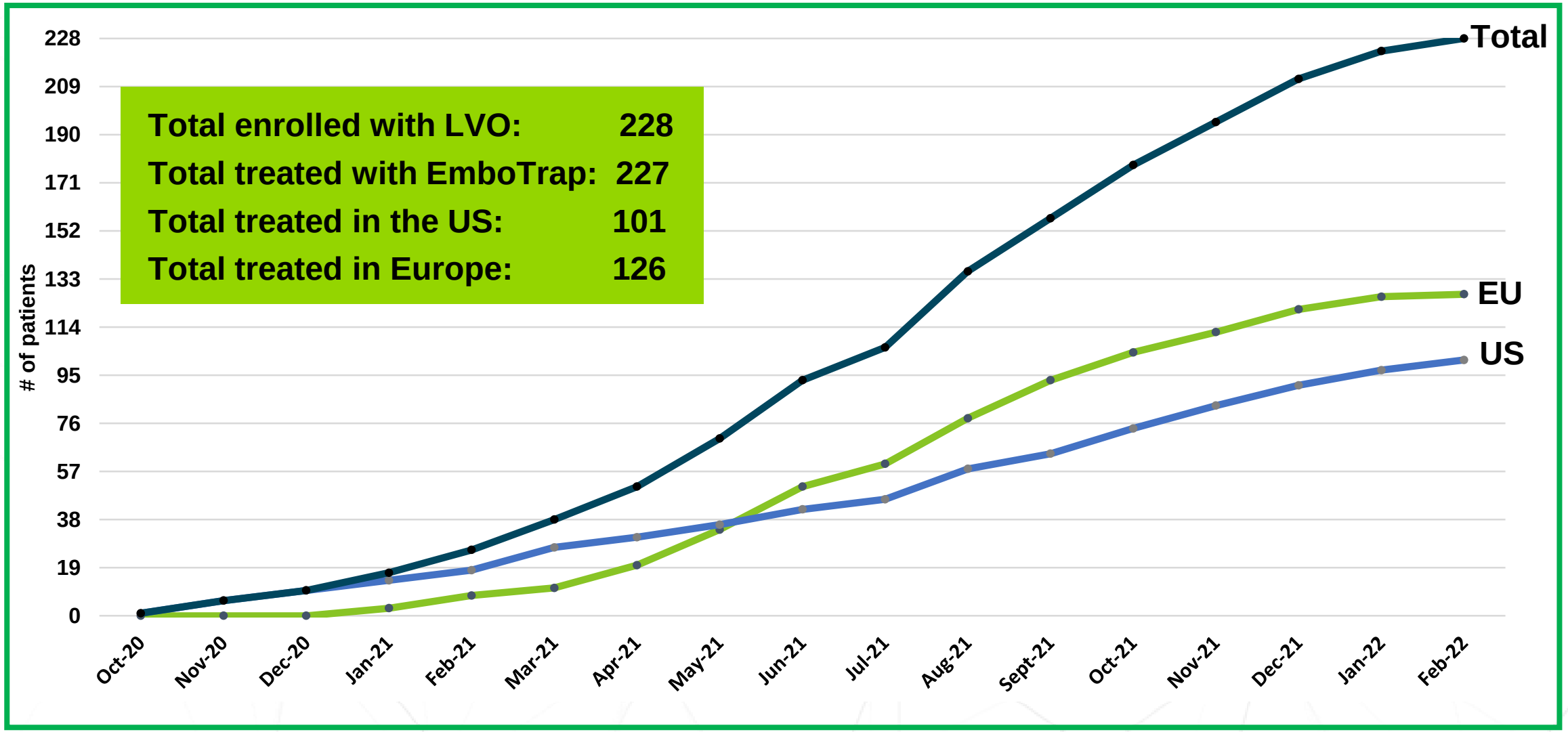
ARISE II RESULTS

ARISE II

RESULTS

ARISE II Enrollment Rate: 228 enrolled

ARISE II



Method: Study Flow Chart

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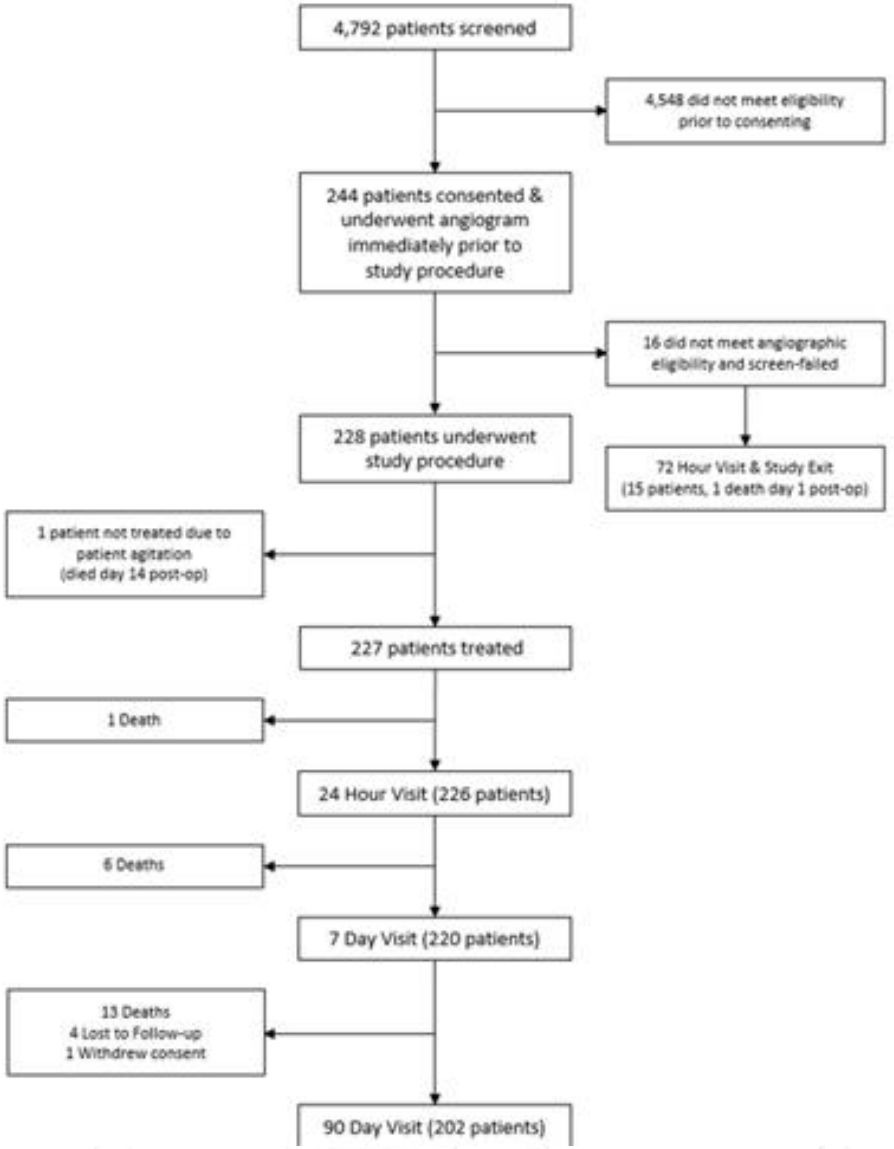
- 5 lost to follow-up
- All patients had angiographic follow-up



DEMOGRAPHIC

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Demographics	ARISE II Treated (N = 227)
Age [years] Mean (SD)	68.0 (13)
Male [%(n)]	45.8% (104)
NIHSS	
Mean (SD)	15.8 (5)
Median	16
Treated with IV-tPA [%,n]	66.1% (150)
Pre Stroke Modified Rankin Score [%(n)]	
0	78% (177)
1	21.6% (49)
2	0.4% (1)

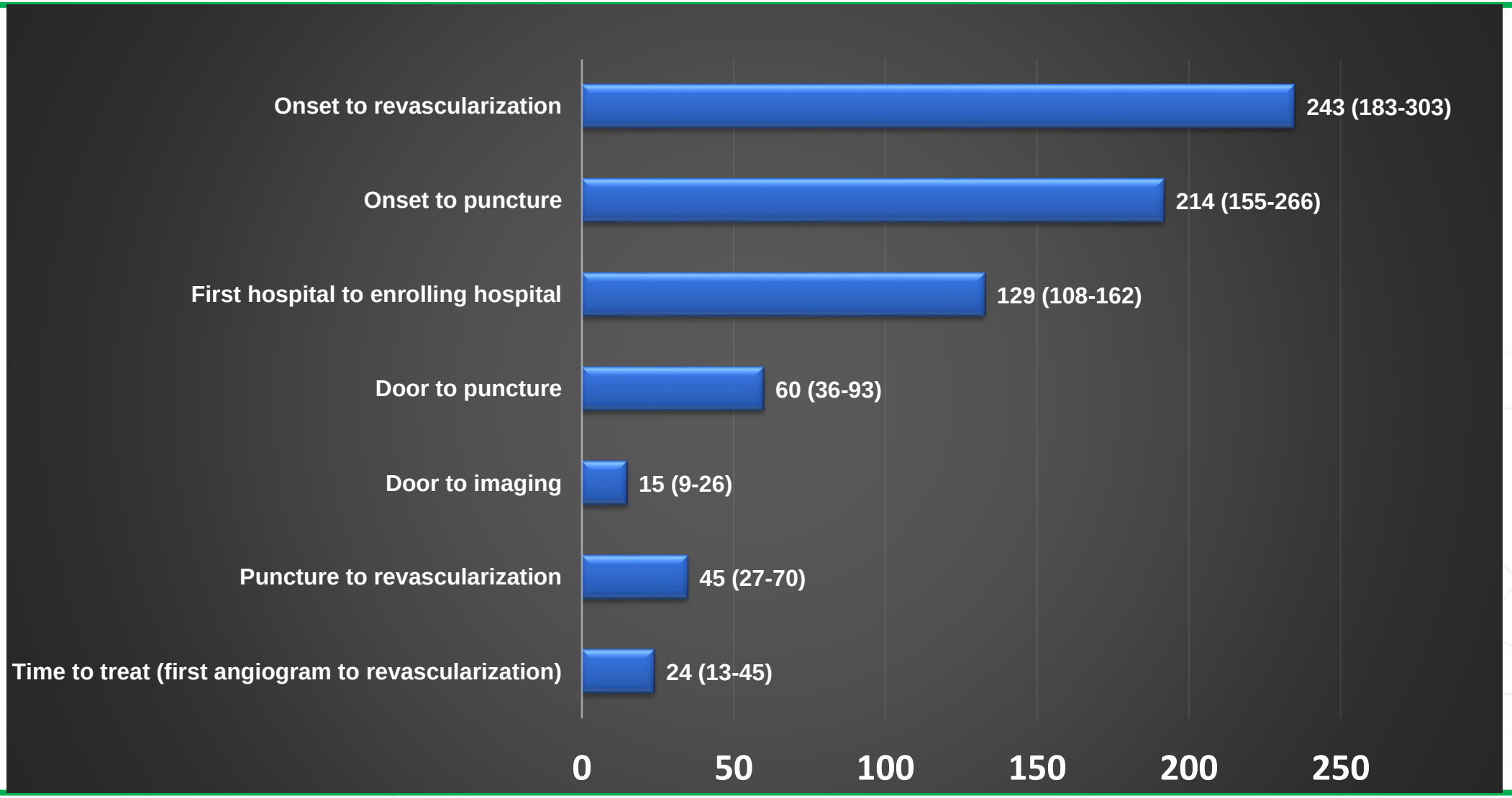
Co-Morbidities

ARISE II

Medical History [% (n)]	Treated (N = 227)
Hypertension	68.3% (155)
Diabetes mellitus	19.8% (45)
Atrial fibrillation	39.6% (90)
Previous Stroke / TIA	18.9% (43)
Previous MI / CAD	19.8% (45)
Dyslipidaemia	43.2% (98)
Smoking	24.7% (56)

RESULTS: Workflow in Median with IQR

ARISE II



Target Vessel Occlusion Per Core Lab

ARISE II

Clot Locations per Core Lab	Treated (N=227)
Anterior Circulation [% (n)]	96% (218)
• Internal carotid artery	15.4% (35)
• M1 middle cerebral artery	55.5% (126)
• M2 middle cerebral artery	25.1% (57)
Posterior Circulation [% (n)]	4% (9)
• Basilar Artery	4% (9)
• Vertebral Artery	0% (0)

Procedural Results

ARISE II

Procedural Information [% (n)]	Treated (N = 227)
Balloon Guide Catheter Use	73.6% (167)
Intermediate Catheter Use	41% (93)

One procedure may have more than one technique

PRIMARY & SECONDARY ENDPOINTS

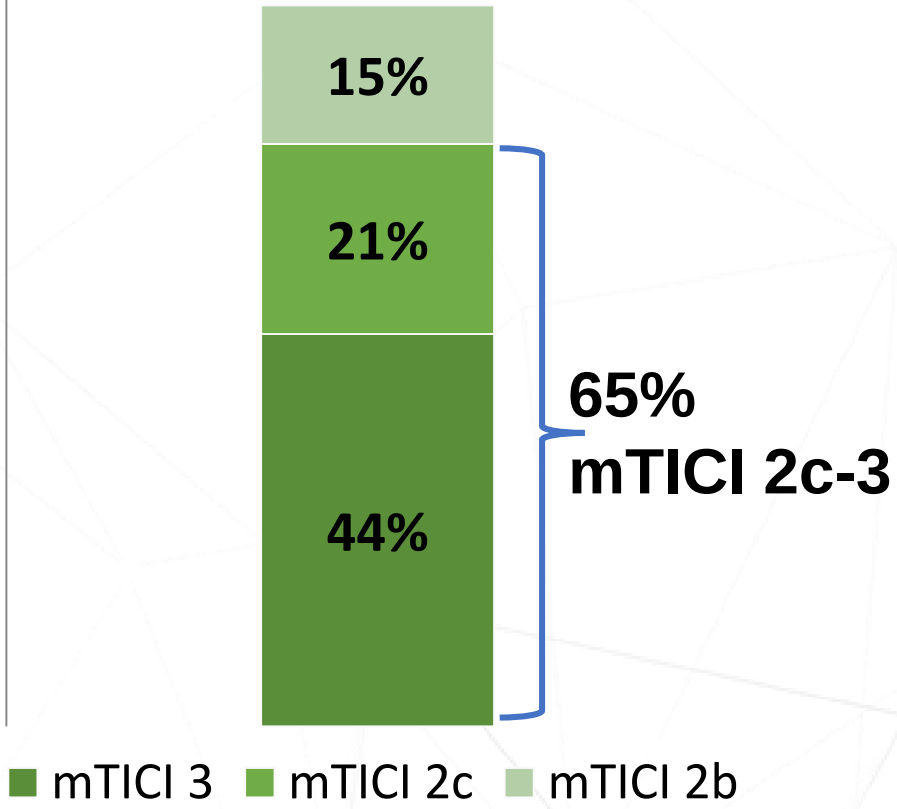
ARISE II

ARISE II PRIMARY AND SECONDARY ENDPOINTS RESULTS

ARISE II Revascularization Outcome

ARISE II

80% mTICI 2b-3

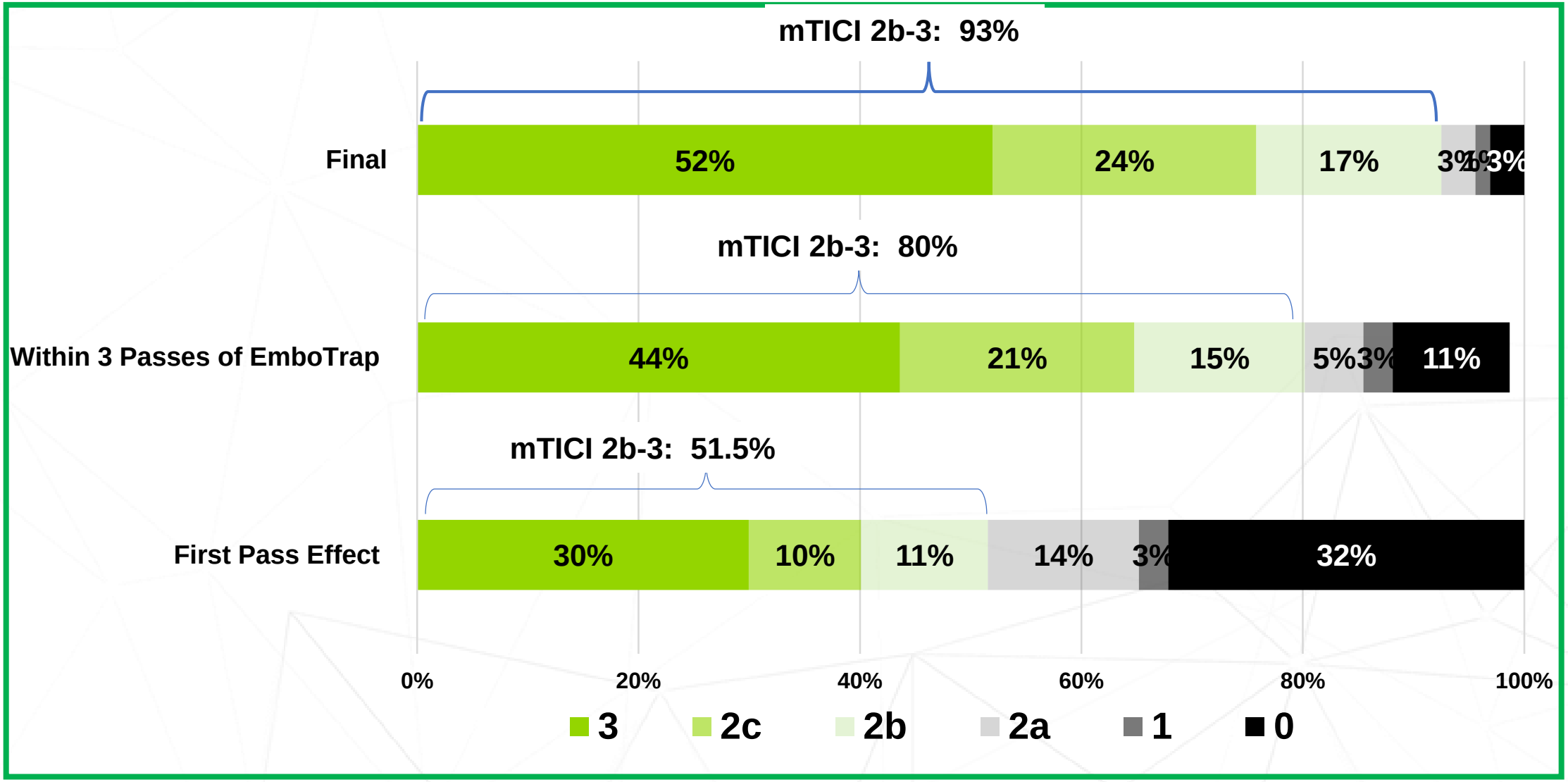


mTICI within 3 passes of EmboTrap	Treated (n=227)*
mTICI 3	**43.6%** (99/227)
mTICI 2c	**21.1%** (48/227)
mTICI 2b	**15.4%** (35/227)
mTICI 2a	**5.3%** (12/227)
mTICI 1	**2.6%** (6/227)
mTICI 0	**10.6%** (24/227)

***The numerator does not sum to 227 as 3 patients had rescue therapy prior to 3rd pass and their angiographic results were not included**

ARISE II Revascularization Outcome

ARISE II

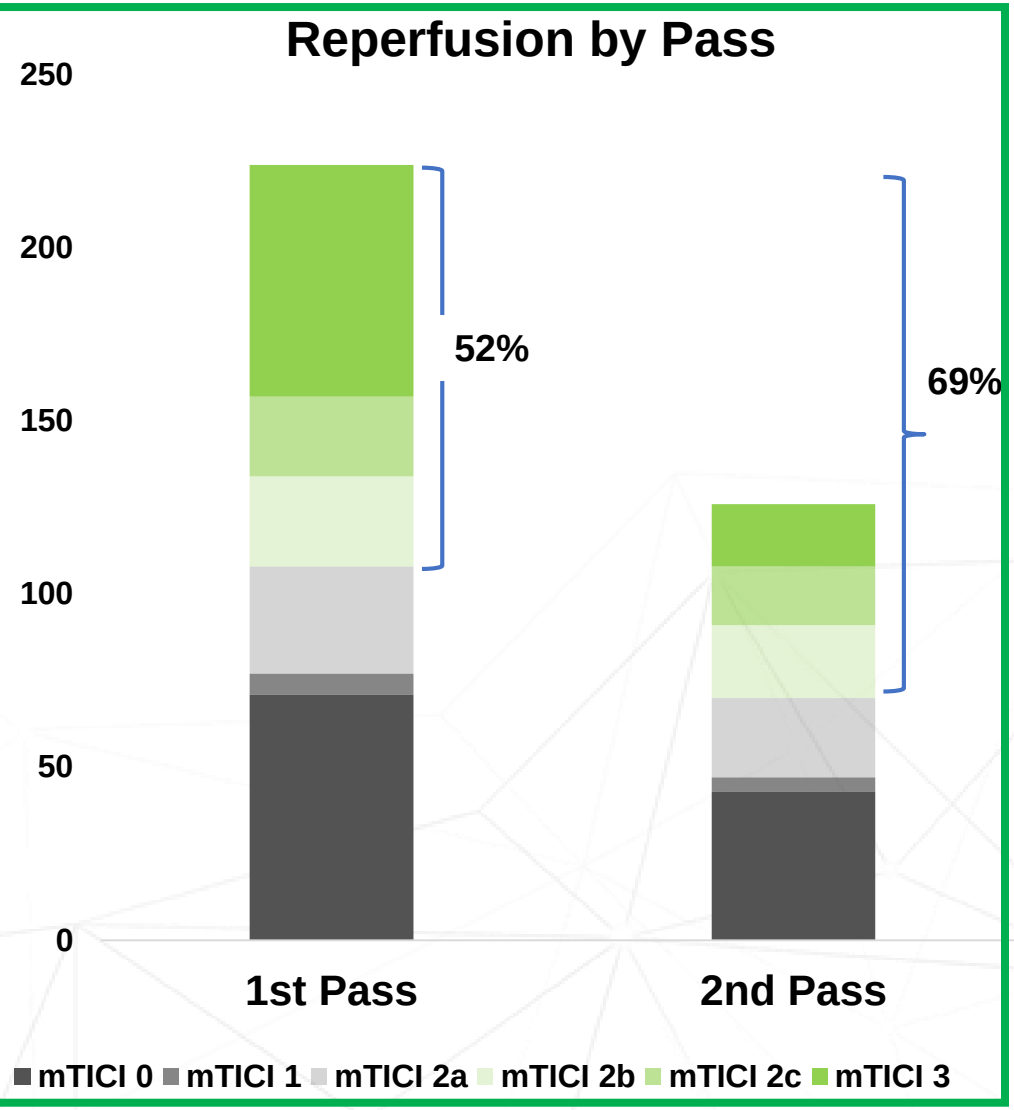


N=227, angiographic outcomes for 3 cases where rescue therapy was used prior to third pass were not included in w/in 3 passes of EmboTrap revascularization

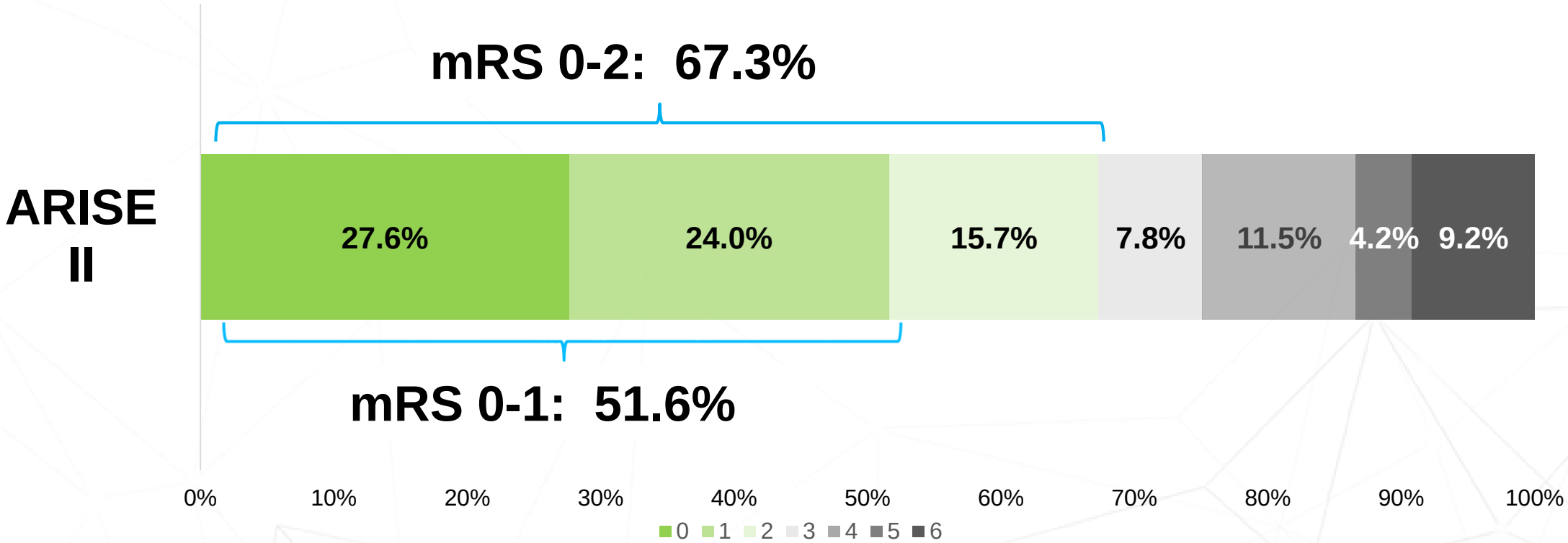
ARISE II Revascularization Rate Per Pass

ARISE II

First Pass Reperfusion with EmboTrap	Treated (n=227)
One-Pass mTICI 2c-3	40.1% (91/227)
One-Pass mTICI 2b-3	51.5% (117/227)



ARISE II Clinical Endpoints



mRS in Treated cohort includes all those treated with rescue therapy but excludes cases where the patient withdrew consent or was lost to follow up with undefined/unknown scores

ARISE II Safety Results

ARISE II

Safety Event	Treated (n=227)
Primary Safety Endpoint sICH within 24 hours in combination with other SADE	5.3% (95%CI: 3-9%)
Neurological deterioration by 4 NIHSS points or more at 24hr	4.5% (95%CI: 2-9%)*
Procedure-related mortality at day 7	0.0% (95%CI: 0-2%)
All-cause mortality at 90 days	9.0% (95%CI: 6-14%)
Embolization into new territory	6.6% (95%CI: 4-11%)

*Absence or presence of neurological deterioration was only documented in 178 patients

ARISE II: Use of other devices (rescue)

ARISE II

Rescue Therapy	Treated (n=227)
Subjects with rescue therapy	19.4% (44/227)
Type of rescue therapy used:	
Mechanical thrombectomy device	16.3% (37/227)
Mechanical pump aspiration	3.1% (7/227)
IA tPA	0.9% (2/227)
Intracranial stenting	0.9% (2/227)
Other	3.5% (8/227)

ARISE II PRIMARY RESULTS

ARISE II

DISCUSSION

Comparison to recent RCT's Final Revasc Success Rate

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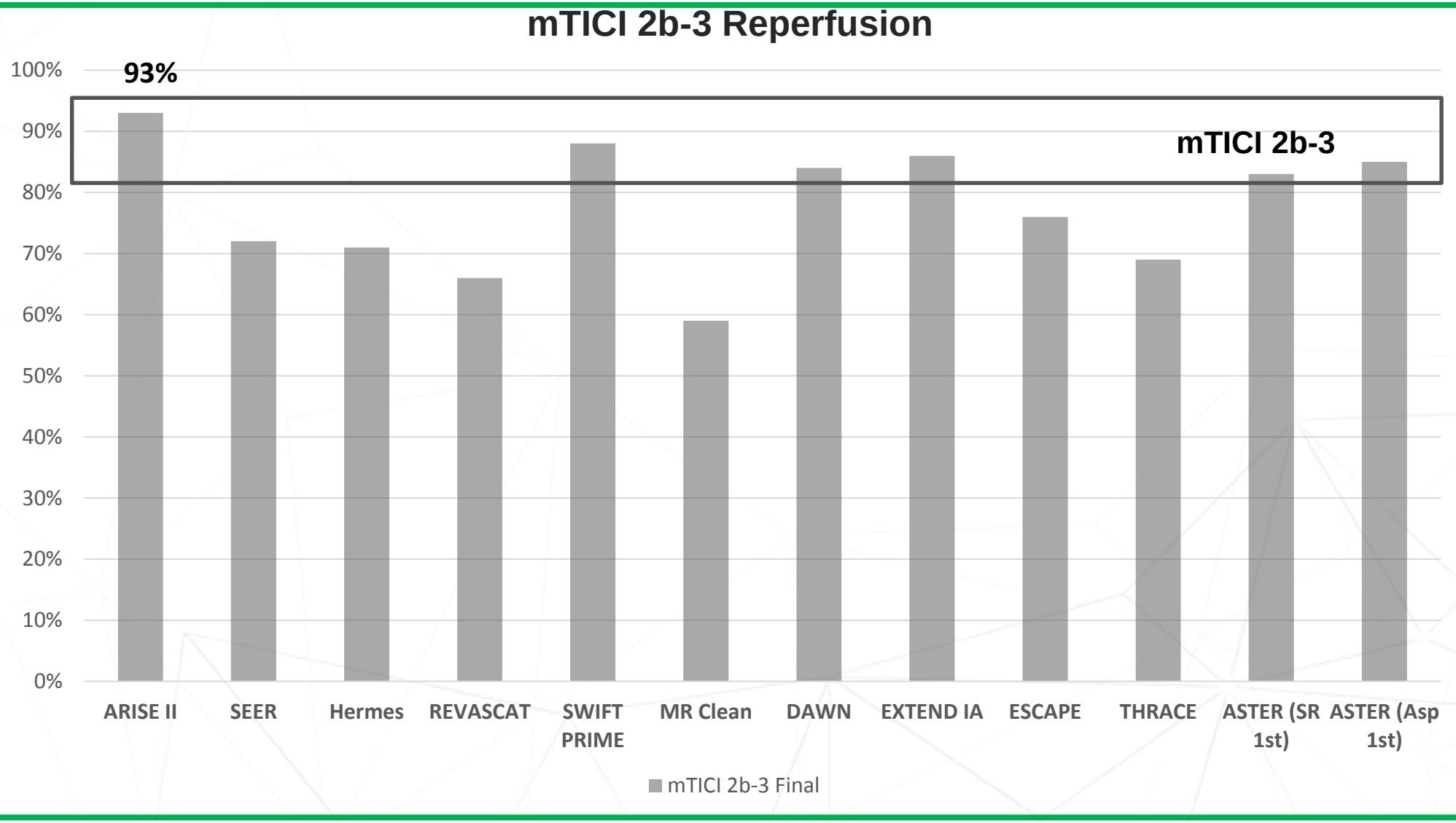

Device Final Complete Revasc Rate vs RCT

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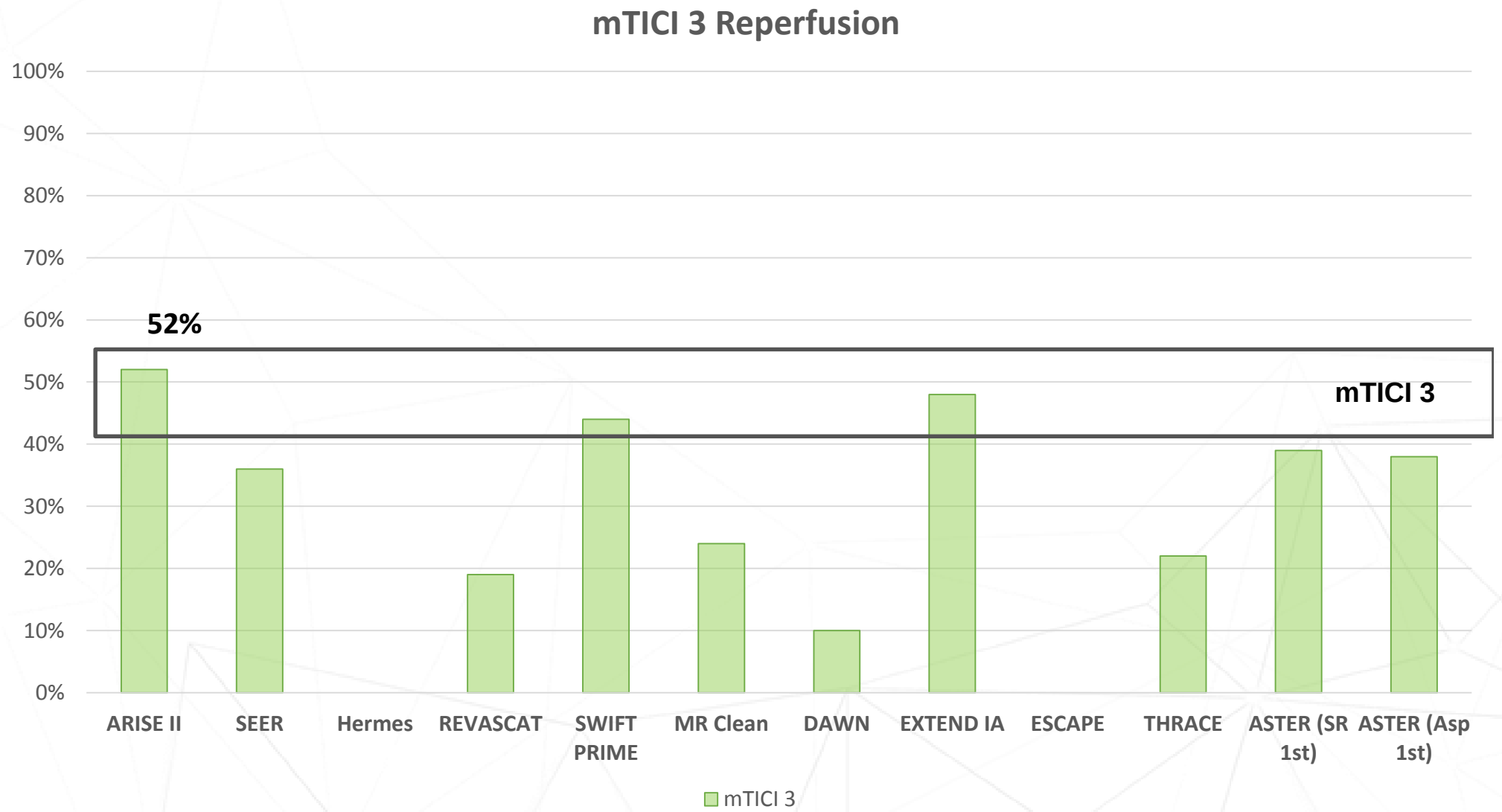
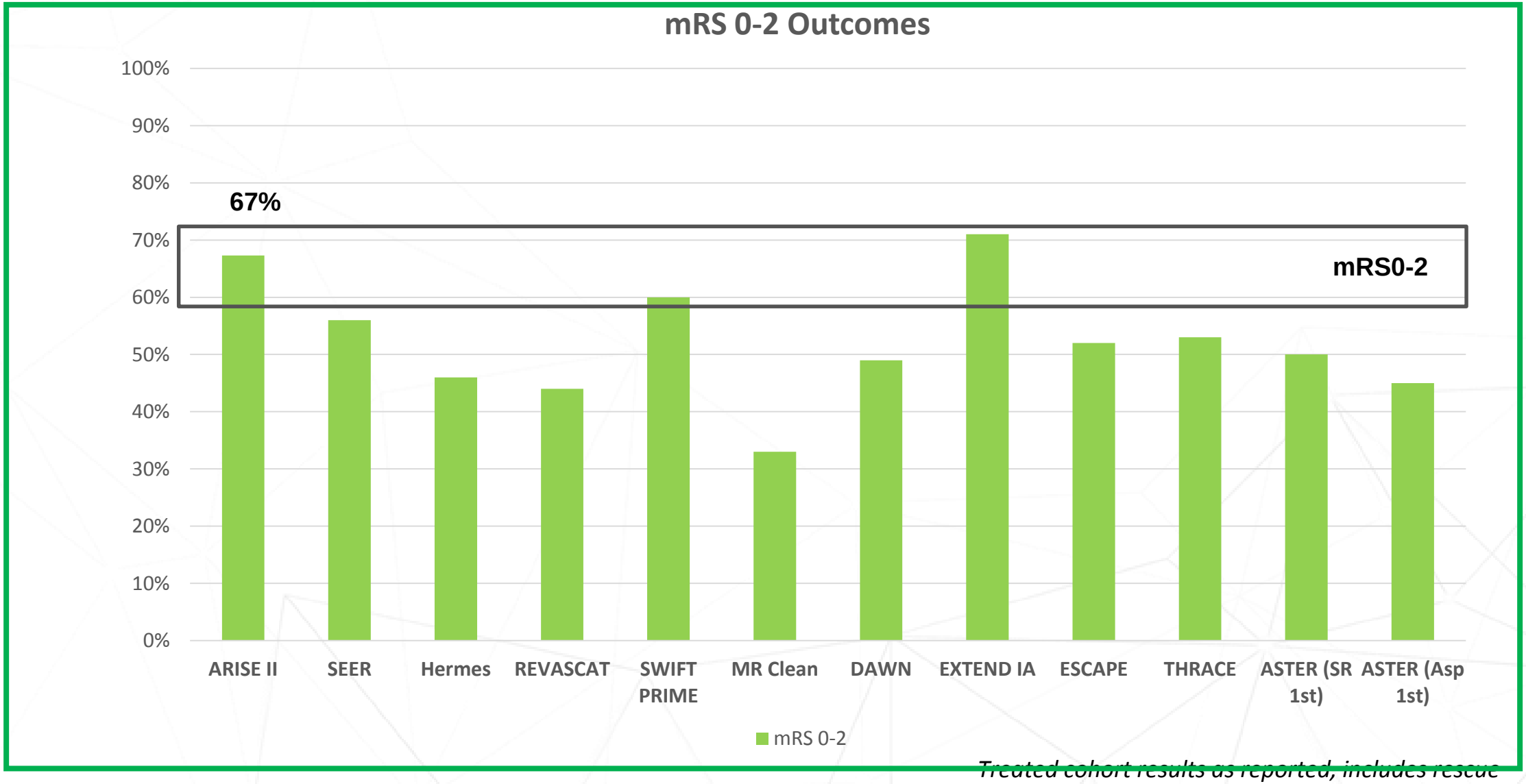


Comparison to recent RCT's: mRS Results

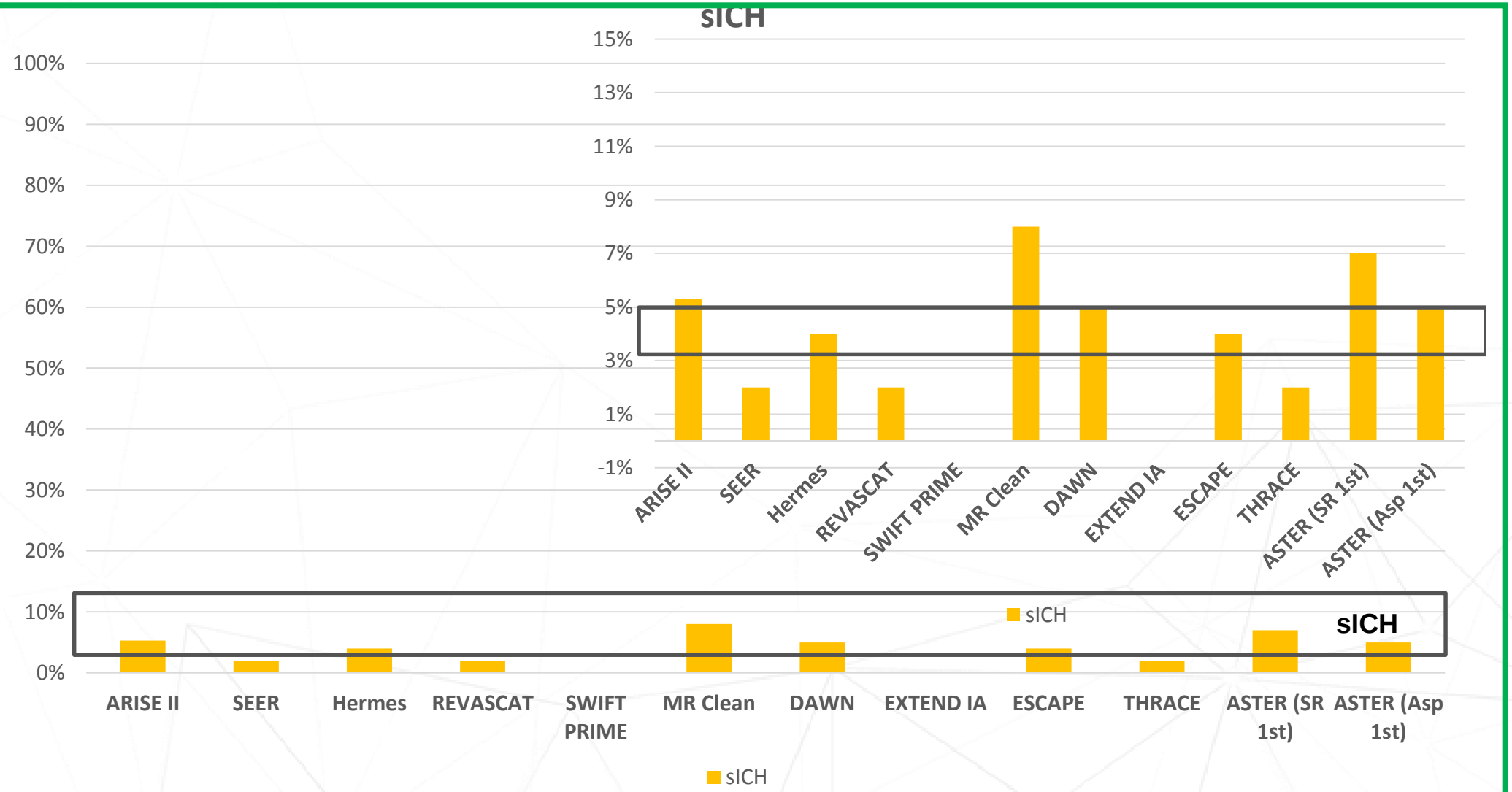
ARISE II



Treated cohort results as reported, includes rescue

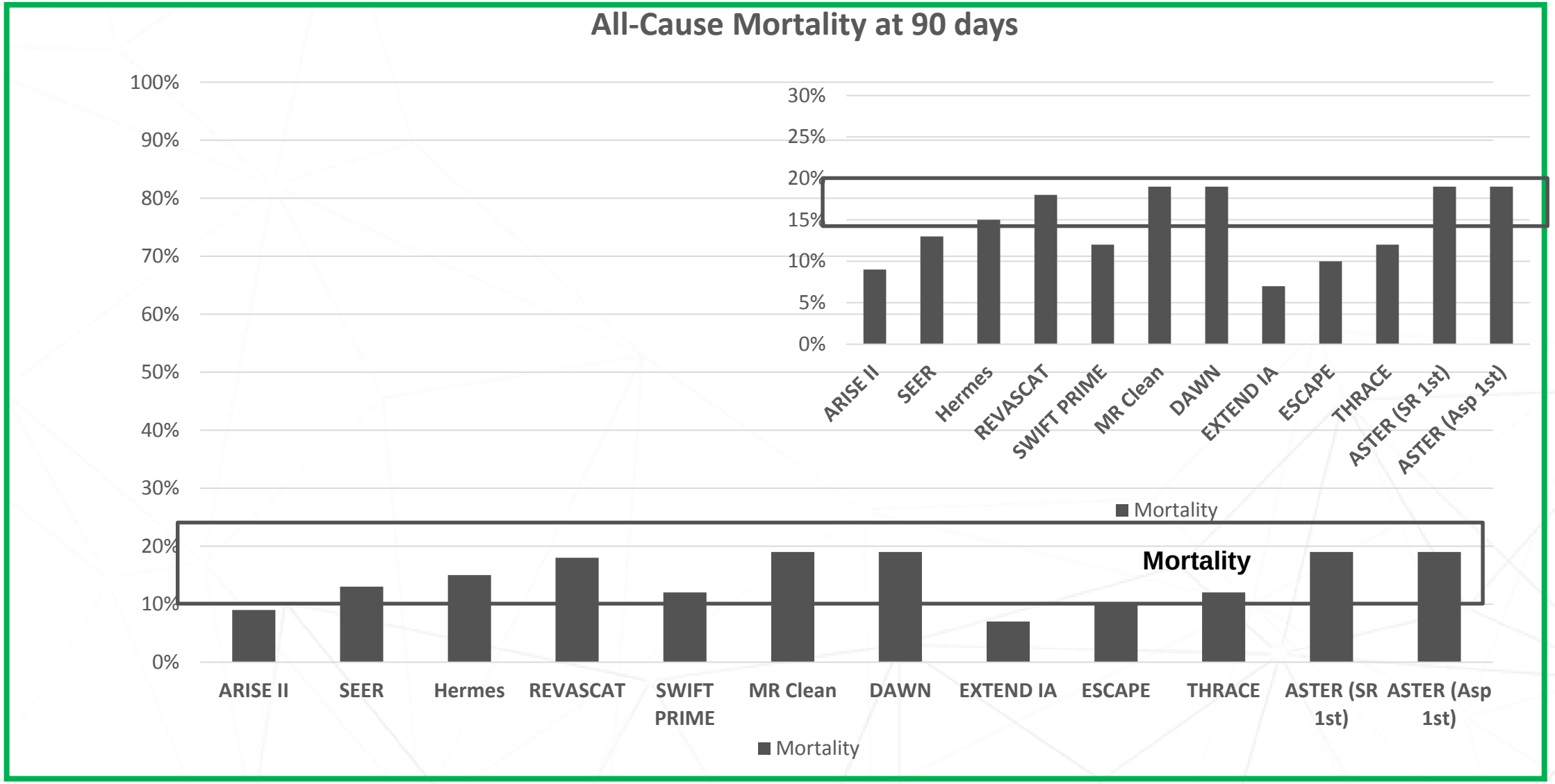
sICH RESULTS COMPARED TO RCT

ARISE II



MORTALITY RESULTS VS RECENT RCT

ARISE II



Summary

ARISE II

- EmboTrap achieved high reperfusion rate in LVO patients:
  - 64.8% mTICI 2c-3 within 3 passes of the EmboTrap
  - **80.2% mTICI 2b-3 within 3 passes (Study Endpoint)**
  - 92.5% mTICI 2b-3 final procedural revascularization
- Promising one-pass success:
  - 51.5% mTICI 2b-3 successful first-pass reperfusion
  - 40.1% mTICI 2c-3 excellent first-pass reperfusion
- Treated patients had good outcomes
  - Functional independence in 67.3% (mRS 0-2)
  - Highly functional independence in 51.6% (mRS 0-1)
  - sICH rate of 5.4% and 90-day Mortality of 9%

One might say…

ARISE II

“Uncertainity is DEFUSED, a new day DAWNs, and we ARISE to meet it with the scineitific COMPASS” Jeff Saver, MD

Thanks to Enrolling Sites PIs, Sub-PIs, CRCs, Patients and Their Families

ARISE II

United States

- OHSU, OR
- UPMC, PA
- Emory, GA
- Mercy St. Vincent Medical Center, OH
- Kaleida Health, Buffalo, NY
- Riverside Radiology, OH
- Banner Desert Med. Center, AZ
- Tennessee Interventional / Erlanger, TN
- Good Samaritan Hospital / Regional Med Ctr, CA
- Mount Sinai, NY
- UCLA, CA

Europe

- Hospital Vall d'Hebron – Spain
- Alfried Krupp Krankenhaus – Germany
- CHRU de Tours – France
- AZ Groeninge – Belgium
- UKSH Kiel – Germany
- Beaumont Hospital – Ireland
- Universitatsklinikum Freiburg – Germany
- Inselspital, Bern - Switzerland