Stanford MEDICINE

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NIH StrokeNet

PREVENTION | TREATMENT | RECOVERY

Funded by a Grant from the National Institutes of Health

DEFUSE 3: Hypothesis

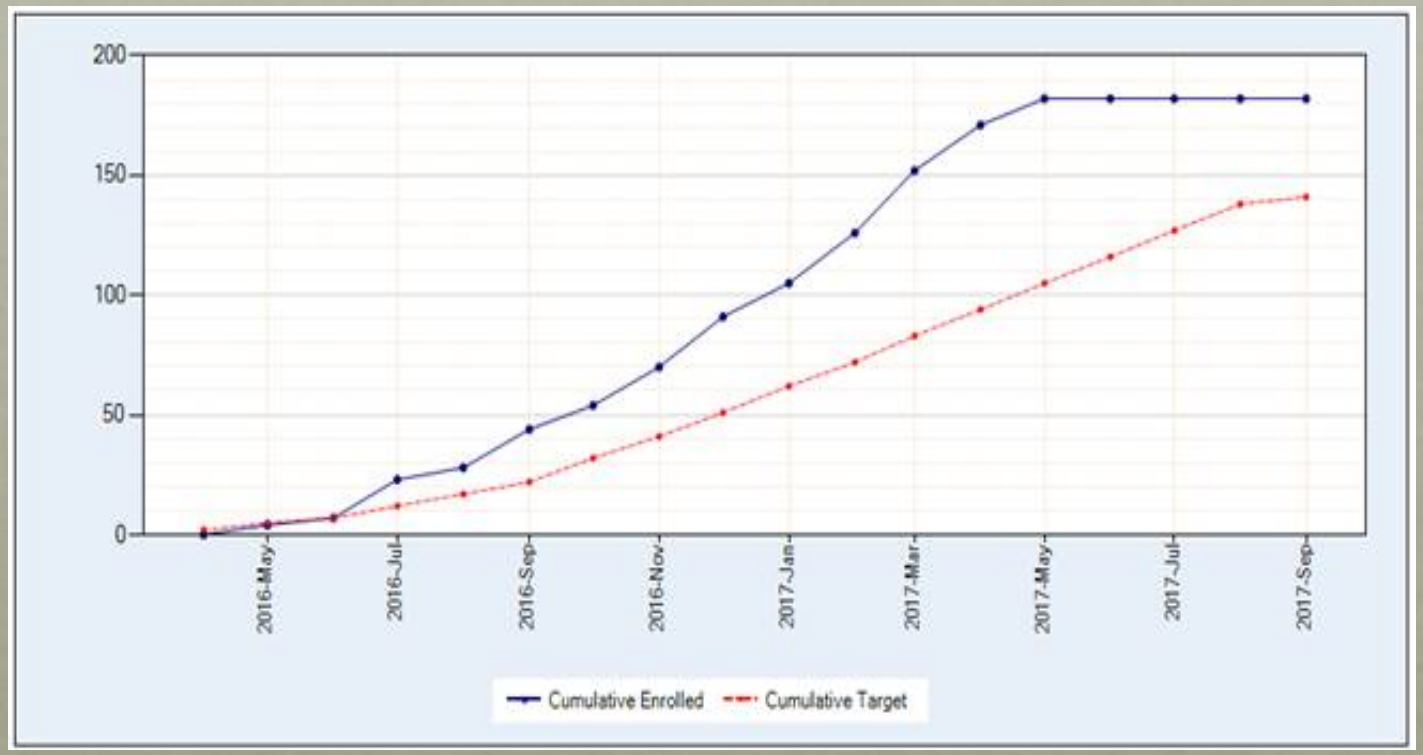
Stroke patients with MCA or ICA occlusion and *salvageable tissue* identified by CT perfusion or MRI benefit from endovascular therapy in the 6-16 hour time-window

DEFUSE 3: Sites & Enrollment

- Number of sites activated to enroll 40
- Number of sites that randomized 38
- Number consented not randomized 114*
- Number of patients randomized 182
- Total patients consented 296

* Most common reasons: no ICA/MI occlusion or core>70 ml

DEFUSE 3: Patient accrual

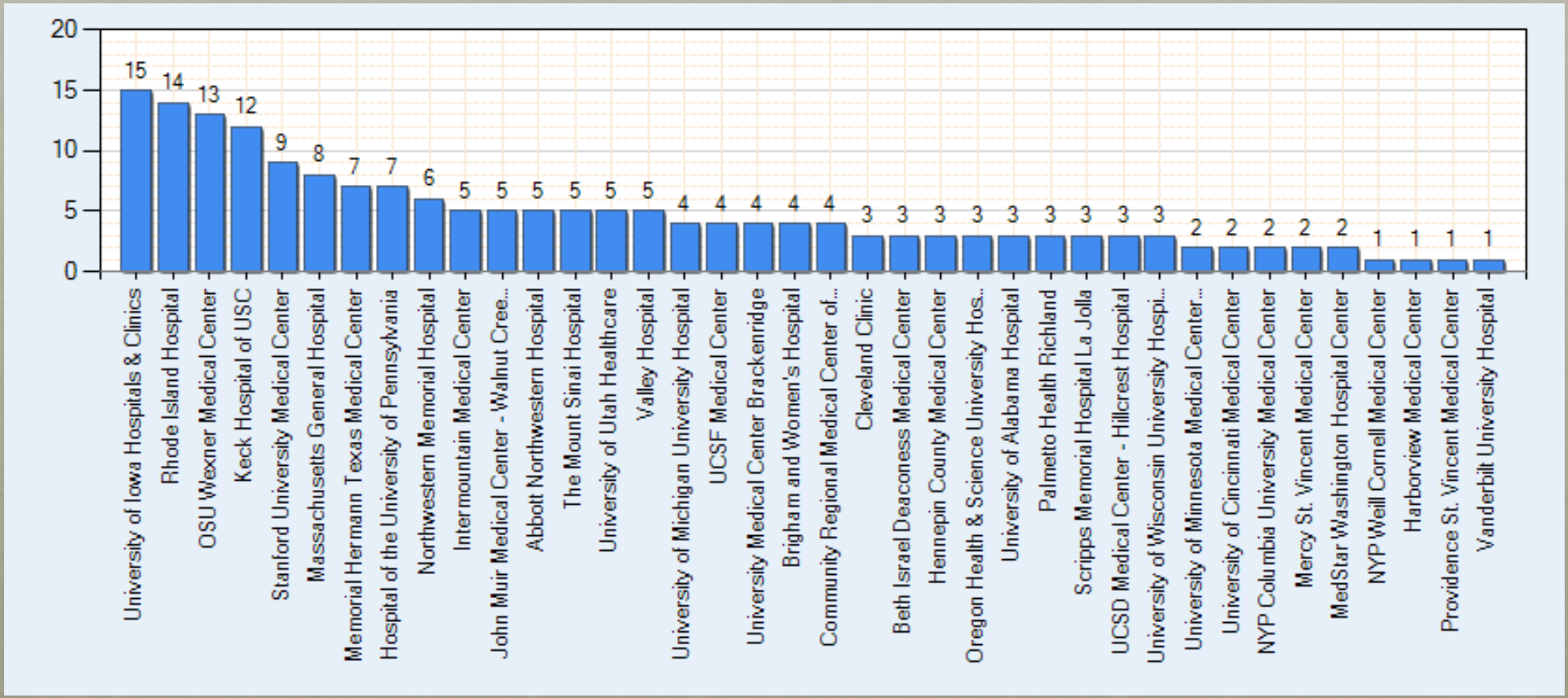


182 patients enrolled in 1 year!

Enrollment rate nearly double projected target

Enrollment > 2X faster than the 6 hour trials

DEFUSE 3: Enrollment by site



40 sites activated; 38 enrolled
0 sites withdrawn

Demographics

	N=182
Age (years) (median, [IQR])	70.5 [59-80]
NIHSS, baseline (median, [IQR])	16 [11-21]
Sex, male (%)	49%
White/Caucasian	87%
Black or African American	8%
Other*	5%
IV-tPA administered	10%

Baseline Imaging Characteristics

	N=182
Qualifying ischemic core volume 0-10 ml 11-25 ml 26-70 ml	 51% 24% 25%
Qualified with baseline DWI/MR perfusion	26%
Qualified with baseline CT/CTA/CT perfusion	74%

Baseline Occlusion

Clot location	
ICA	26%
M1	64%
M2	5%

Patient Presentation

	N=182
Time from last well to randomization	
Mean ± SD Median (Q1, Q3) Range (min, max)	10.8 ±2.5 hrs 10.8 (8.7, 12.7) (6.1, 15.9)
Wake-up stroke	47%
Known onset time	36%

DEFUSE 3: May 2017

- May 16: Positive DAWN results presented at ESOC
  - 60% D3 pts met DAWN criteria
- May 17: "Equipoise survey" sent to D3 investigators
- May 24: StrokeNet CIRB halted enrollment for "DAWN-eligible" patients
- May 26: DEFUSE 3 DSMB meeting

May 26 DSMB meeting

- D3 Exec Committee recommended halting the study:
  - Survey results: many investigators had lost equipoise
  - "Non-DAWN" criteria not feasible
  - Concern regarding biased accrual if study not halted
  - Central IRB potentially unlikely to allow study to continue
- DSMB (closed session) recommends halting the trial
- NIH did not accept DSMB recommendation
  - Places study on hold and requests modified SAP with early interim and option to continue study if stopping rule not met

June 2017

- June 3: Modified SAP proposed interim analysis stopping rule: 1-sided alpha of $P < 0.023$
- DSMB meeting June 24; stopping rule changed to O'Brien-Flemming spending function (2-sided efficacy Boundary Z-scale ± 3.018)
- Data reviewed and study stopped for efficacy
- No evidence of imbalances or safety concerns

DEFUSE Large Core Study

- June 28: DEFUSE 3 request to modify protocol to evaluated large core/large mismatch patients denied
- Sept 1: New study, DEFUSE M, presented to NIH ESC
- DEFUSE M grant not approved to be submitted for peer-review; changes in design requested
- Request: fully define the limits of EVT (i.e., when do you lose benefit?)

DEFUSE 3 PRESENTATIONS

- International Stroke Conference Los Angeles
  - Primary results on Wednesday January 24th
  - Subgroups and Endovascular presentations (25th /26th)
- Tuesday January 23: DEFUSE 3 Investigators meeting
  - 7 pm-9 pm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