



Main Line Health[®]

Well ahead.[®]

CREST-2

Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis

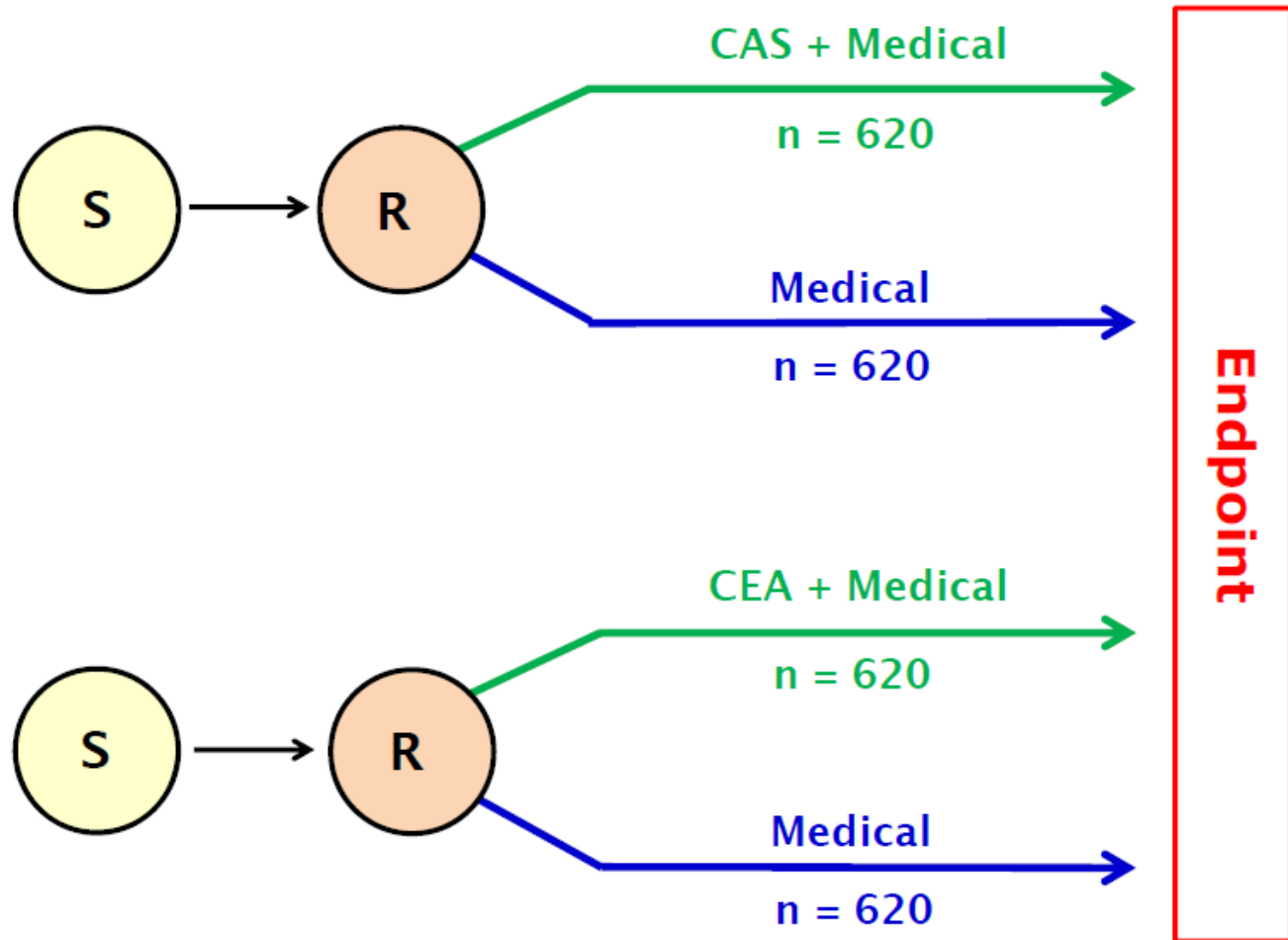
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Services, Main Line Health
President, Lankenau Heart Institute
Wynnewood, PA
USA

CREST-2

- Two parallel multi-center randomized, observer blinded endpoint trials
- NINDS funded clinical trial (U01 NS080168)
- Notice of award received March 11th, 2014
- Clinical Coordinating Center: Mayo Clinic Florida
- Statistical and Data Coordinating Center: University of Alabama at Birmingham

CREST-2: Parallel Study Design

(n = 1,240 in each trial)



S = Screened
R = Randomized

Endpoint = all stroke & death in first 30 days and ipsilateral stroke thereafter up to 4 years.

CREST 2: Primary Aims

- In patients with $\geq 70\%$ asymptomatic stenosis, to assess:
- The treatment differences between medical management and CEA
- The treatment differences between medical management and CAS

CREST 2: Secondary Aims

To assess:

- Differences in cognitive function in patients randomized to intensive medical management compared to those randomized to CEA or CAS at 4 years of follow-up.
- Differences in major stroke events at 4-years
- Differences in primary outcomes affected by age, sex, severity of carotid stenosis, risk factor level, and duration of asymptomatic period.

Definition: $\geq 70\%$ Stenosis

PSV* ≥ 230 cm/second on DUS,
plus one of the following 4 criteria:

- EDV** ≥ 100 cm/second on DUS or
- IC / CC PSV*** ≥ 4.0 on DUS or
- $\geq 70\%$ stenosis on MR angiogram or
- $\geq 70\%$ stenosis on CT angiogram

*peak systolic velocity

**end diastolic velocity

***internal carotid / common carotid artery peak systolic velocity

Which Trial?

Which Procedure?

From overall (sx and asx) population in CREST 1:

- For ages 50-74 years, no favored procedure
- For ages <50 years, CAS is the favored procedure
- For ages >74 years, CEA is the favored procedure
- BUT, in CREST asymptomatic patients had few events, so there were wide confidence intervals

So, the choice of CEA or CAS cannot be mandated in CREST-2...

...and individual patient characteristics and preferences may supersede guidelines

Selected Exclusions for CEA



Neck
dissection



Tracheostomy
stoma

Radical neck dissection

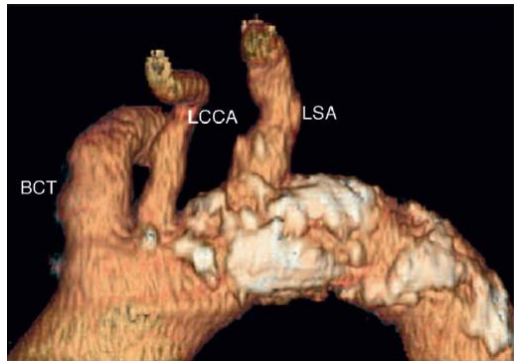
Surgically inaccessible
lesions

Neck anatomy limiting
surgical exposure

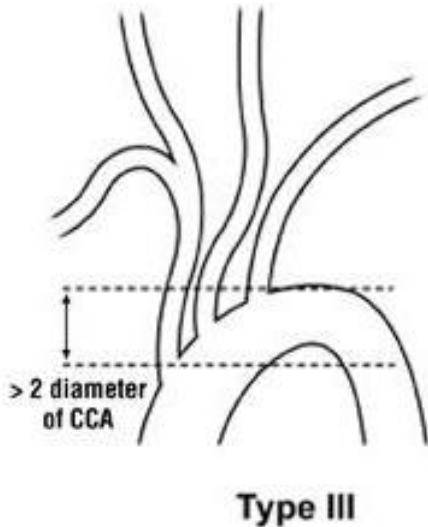
Tracheostomy stoma

Laryngeal nerve palsy
contralateral to target
vessel

Selected CAS Exclusions: Generally will require CTA or MRA



Severe atherosclerosis of the aortic arch or origin of the innominate or common carotid arteries



Type III, calcified aortic arch anatomy

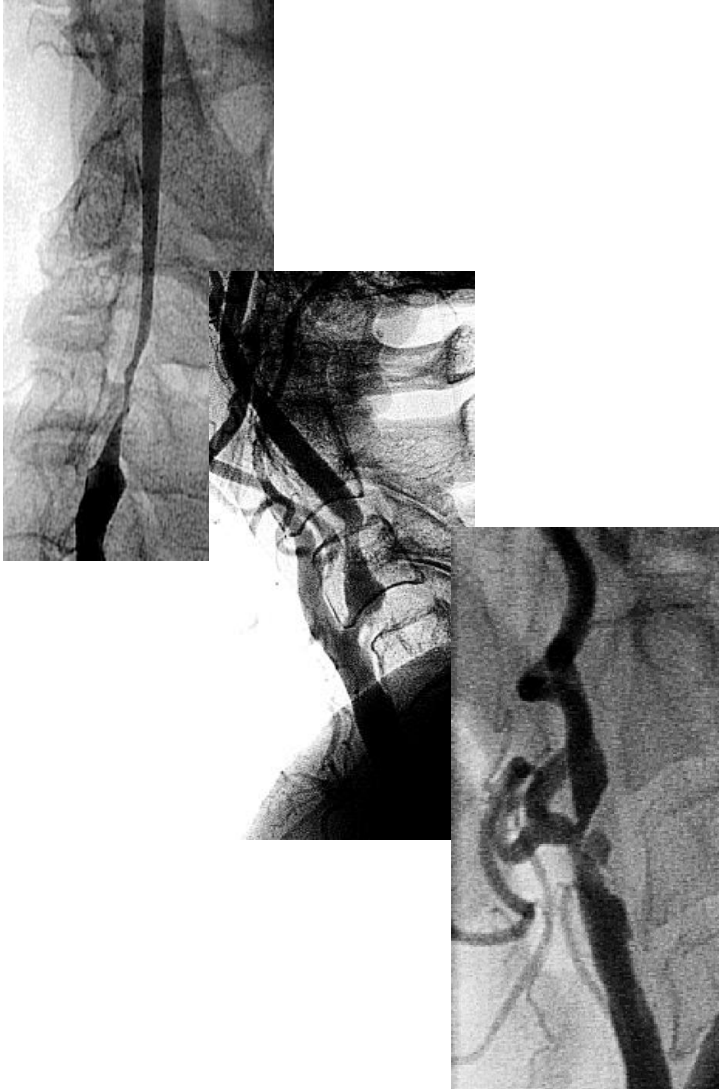
Angulation or tortuosity ($\geq 90^\circ$) of the innominate, common or internal carotid artery

Selected CAS Exclusions

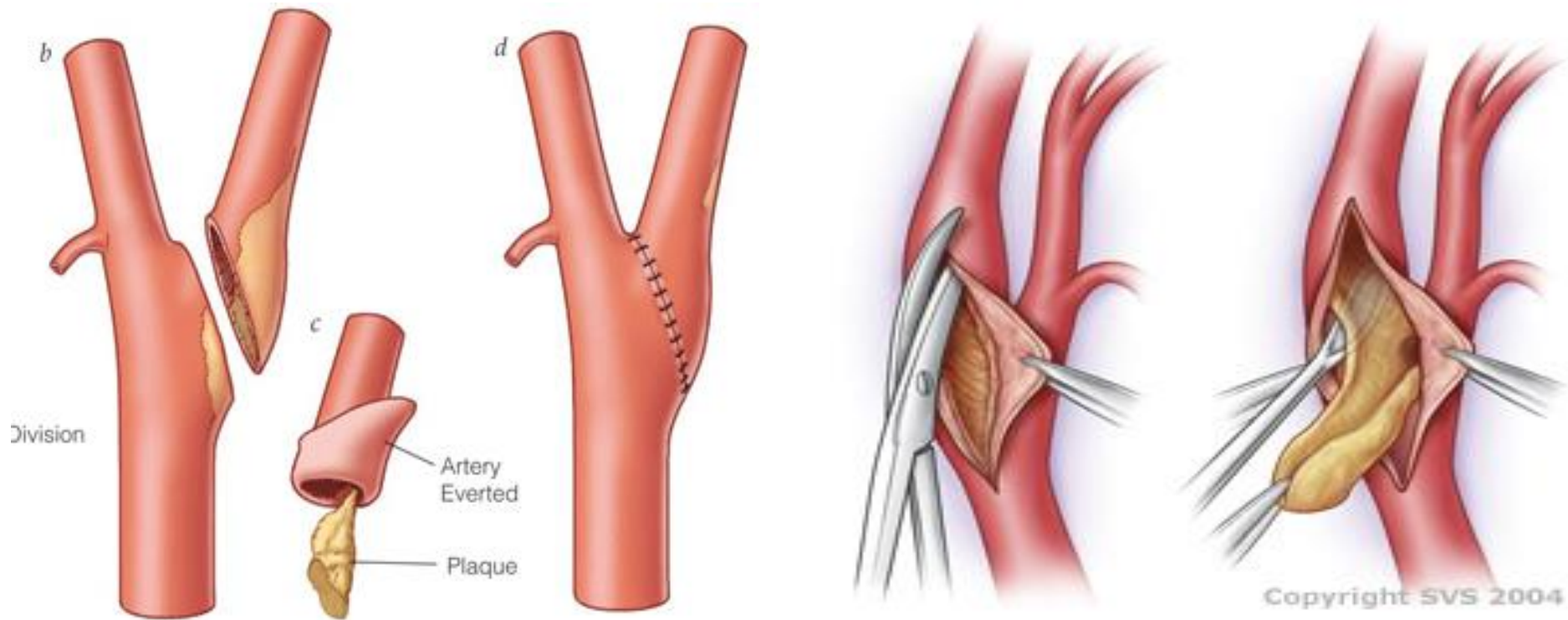
Excessive or circumferential calcification of the stenotic lesion

Lesions >20 mm in length, sequential lesions, and narrow-mouth ulcers

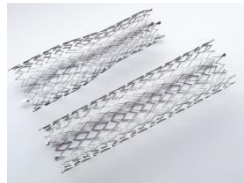
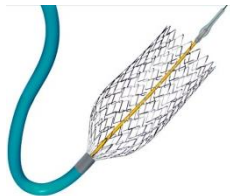
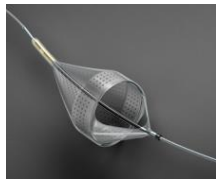
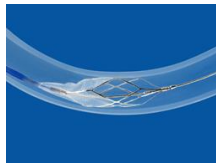
Inability to deploy or utilize an FDA-approved Embolic Protection Device (EPD)



JUST LIKE CREST this is not a ONE-CEA trial



UNLIKE CREST, This is not a One CAS Trial



Company	Stent	Embolic Protection Device
Abbott	RX Acculink [®]	RX Accunet [®]
	Xact Stent	Emboshield Nav ⁶
Boston Scientific	Carotid WALLSTENT [™]	FilterWire EZ [™]
Cordis-a Cardinal Health Company	PRECISE PRO RX [®] Nitinol Stent	ANGIOGUARD [®] RX Emboli Capture Guidewire
Medtronic/Covidien	Protege [®] RX	SpiderFX [®]
		MO.MA [®] Ultra

Medical Management

- Patients in both trials will take aspirin 325 mg per day for the entire follow-up period (CAS patients will also take clopidogrel per protocol).
- Primary risk factors: systolic blood pressure and LDL cholesterol
 - Managed by the study neurologist/internist
 - Target systolic blood pressure <140 mmHg
 - Target LDL <70 mg/dl

Medical Management

- Secondary risk factor targets:
 - Non-HDL cholesterol <100 mg/dl.
 - Hemoglobin A1c <7.0%.
 - Smoking cessation.
 - Targeted weight management.
 - > 30 minutes of moderate exercise 3 times a week.

CREST 2: Covered Medications

- **Antiplatelet agents**
 - clopidogrel
- **Statin**
 - atorvastatin
- **Anti-hypertensive Rx**
 - One drug from each major class will be available: diuretic, ACE inhibitor, potassium-sparing diuretic, angiotensin receptor blocker, beta blocker, vasodilator, central alpha agonist, long-acting calcium channel antagonist

INTERVENT

- Lifestyle management and cardiovascular disease risk reduction program.
- Incorporates SAMMPRIS targets and national guidelines.
- Provides individualized risk factor counseling telephone sessions at regular intervals:
 - twice a month for 12 weeks.
 - monthly thereafter.
- Case Managers at INTERVENT call center, Savannah GA.

Cognitive Outcome

- Is the **change of cognitive function** from baseline to 48 months no worse among those in the MEDICAL cohort compared to the CEA/CAS cohorts?
 - *Cognitive function may be a surrogate for TIA and/or asymptomatic brain injury*
- Computer-aided telephonic assessment by team at University of Alabama.

CREST 2: Status update

Site Selection Committee Report Bart Demaerschalk/Eldina Kadiric

- 203 Invitation packets have been sent out
- 116 CREST-2 approved sites who are approved to move forward with IRB submission
 - 35 of these are StrokeNet sites
- 79 sites with Green Light Letters
 - 23 of these are StrokeNet sites

CREST 2: Status update

Recruitment and Retention Kevin Barrett/Mary Longbottom

- **2** enrolled in 2014; **152** enrolled in 2015; **1** enrolled in 2016 for a total of **155**

- 65 CEA Trial
- 90 CAS Trial
- 41% women
- 7% minorities

Inerventional site selection Sothear Luke

- 87 approved
- 136 conditionally approved

CREST 2: Status update

- LDL:
 - 41% at ≤ 70 at baseline
 - 53% at 44 days
 - 68% at 4 months
- Systolic BP:
 - 57% ≤ 140 at baseline
 - 71% at 44 days
 - 81% at 4 months

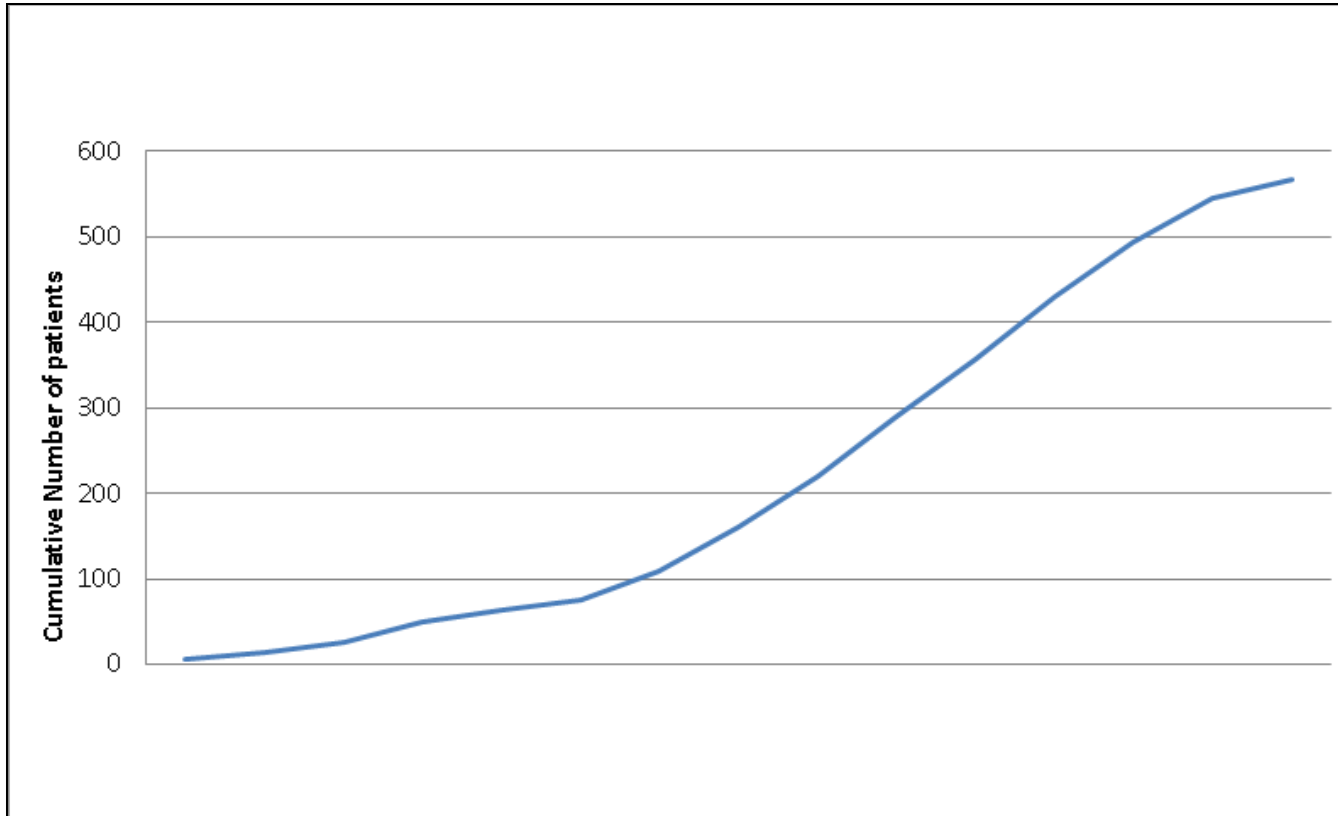
C2R Objectives

To assure:

- Rapid initiation and completion of enrollment in CREST-2
- That CAS is performed safely and with good outcomes by adequately experienced operators

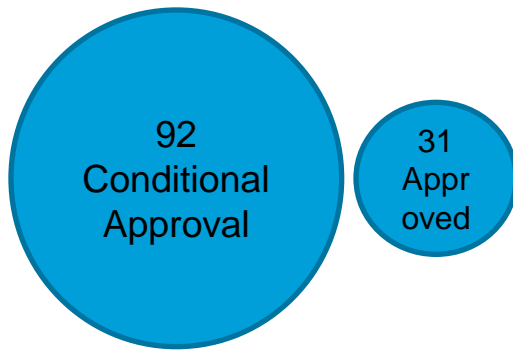
C2R Patient Enrollment

C2R total enrollment	565
- Data collection through SVS-VQI and C2R	311
- Data collection through NCDR-PVI and C2R	254

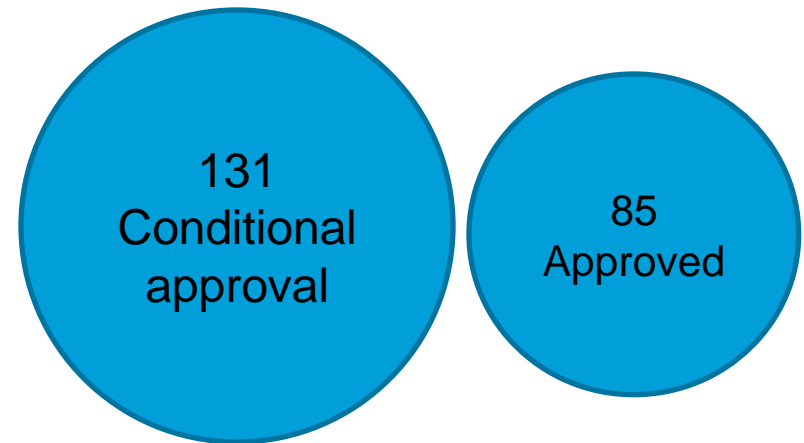


Acceleration of CREST 2 Physician Approval

February 1, 2015



December 1, 2015



Thank you