CREST-2
Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis

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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

CAS + Medical
n = 620

Medical
n = 620

CEA + Medical
n = 620

Medical
n = 620

Endpoint

S = Screened
R = Randomized

Lankenau Heart Institute
Main Line Health

Endpoint = all stroke & death in first 30 days and ipsilateral stroke thereafter up to 4 years.
CREST 2: Primary Aims

• In patients with ≥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: ≥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
- ≥ 70% stenosis on MR angiogram or
- ≥ 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

- 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 (≥90°) 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

<table>
<thead>
<tr>
<th>Company</th>
<th>Stent</th>
<th>Embolic Protection Device</th>
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</thead>
<tbody>
<tr>
<td>Abbott</td>
<td>RX Acculink®</td>
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<tr>
<td></td>
<td>Xact Stent</td>
<td>Emboshield Nav⁶</td>
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<tr>
<td>Boston Scientific</td>
<td>Carotid WALLSTENT™</td>
<td>FilterWire EZ™</td>
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<td>Cordis-a Cardinal Health Company</td>
<td>PRECISE PRO RX® Nitinol Stent</td>
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<td>SpiderFX®</td>
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<td>MO.MA® Ultra</td>
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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  Sohear 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

<table>
<thead>
<tr>
<th>C2R total enrollment</th>
<th>565</th>
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<tr>
<td>- Data collection through SVS-VQI and C2R</td>
<td>311</td>
</tr>
<tr>
<td>- Data collection through NCDR-PVI and C2R</td>
<td>254</td>
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![Graph showing cumulative number of patients](image)

Lankenau Heart Institute
Main Line Health
Acceleration of CREST 2
Physician Approval

February 1, 2015

92 Conditional Approval

31 Approved

December 1, 2015

131 Conditional approval

85 Approved
Thank you