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

VEITH
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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

Primary endpoint: proportion of patients who experienced any stroke or death within 44 days of randomization or ipsilateral ischemic stroke thereafter up to 4 years.

Secondary Aims
In patients with ≥70% asymptomatic stenosis, 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.

Definitions for ≥70% Stenosis
Peak systolic velocity ≥230 cm/sec on Duplex ultrasound AND
At least one of the following:
- End diastolic velocity ≥100 cm/sec or
- ICA/CCA peak systolic velocity ratio ≥4.0
- ≥70% stenosis on MR angiogram or
- ≥70% stenosis on CT angiogram

Two Concurrent Two-arm Trials

Disclosures
I have nothing to disclose
Selected Exclusions for CEA and CAS

- Radical neck dissection
- Surgically inaccessible lesions
- Neck anatomy limiting surgical exposure
- Tracheostomy stoma
- Laryngeal nerve palsy contralateral to target vessel

Selected Exclusions for Stenting

- Severe atherosclerosis of the aortic arch or origin of the innominate or common carotid arteries
- Type III, calcified aortic arch anatomy
- Lesions >30 mm in length, sequential lesions, and narrow-mouth ulcers
- Angulation or tortuosity (≥90°) of the innominate, common or internal carotid artery
- Inability to deploy or utilize an FDA-approved embolic protection device

Procedural Latitude

<table>
<thead>
<tr>
<th>Stent</th>
<th>Embolic Protection Device</th>
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<tr>
<td>Acculink</td>
<td>RX Accunet OR</td>
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<tr>
<td>Xact Stent</td>
<td>EmboShield Nav6</td>
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<td>Carotid Wallstent</td>
<td>FilterWire EZ</td>
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<tr>
<td>Protege® RX</td>
<td>SpiderFX®</td>
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<tr>
<td>PROGRESS® Nitril Stent</td>
<td>ANGIOGUARD™ Emboli-Capture Guidewire</td>
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CREST-2 Medical Management

Patients in both trials will take aspirin 325 mg/d for the entire follow-up period (CAS patients will be on dual antiplatelet therapy for 1 month post-procedure).

Primary Risk Factor Targets
- Systolic BP <140 mm Hg
- LDL cholesterol <70 mg/dl

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

Lifestyle Coaching

- Lifestyle management will be done by case managers at INTERVENT, Savannah, GA.
- Incorporates SAMMPRIS targets and national guidelines.
- Provides individualized risk factor counseling telephone sessions at regular intervals:
  - Months 1 to 3: 2 per month
  - Months 4 to 12: 1 per quarter
  - Months 12 to close: 2 per year

Cognitive Testing

- Word list learning
- Word list learning (recall)
- Animal learning
- Letter fluency
- Digit span (forward and backward)
- Center for Epidemiologic Studies-Depression-4
- Short Form Health Survey 12 (SF-12)
Interventional Management Committee

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<td>Not Approved</td>
<td>161</td>
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<tr>
<td>Pending</td>
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<td>Conditionally</td>
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As of November 9, 2015

Surgical Management Committee

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<tr>
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</tr>
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</table>

As of November 9, 2015

Surgeons greenlighted to perform CEA
- Vascular Surgeons: 138
- Neuro Surgeons: 14
- Vascular Surgeons: 22
- Other: 48

Enrollment Trends
- CEA lagging behind CAS trial
- Can we commit to reimbursement for patients randomized to medical treatment in the CEA trial??

CAS vs CEA enrollment
- 75 in CAS
- 59 in CEA
Vascular Imaging Core

- 85 clinical centers
- 387 vascular technologists reviewed
- 16 not approved
- 371 (95.8%) credentialed

- 24 hour turnaround time for reporting of “doubtful” tests
- Send in any ultrasounds you have questions on

CREST-2 Registry

- Objectives
  - Rapid initiation and completion of enrollment in CREST-2
  - That CAS is performed by adequately experienced operators within the CREST-2 trial and the companion registry

- Milestones
  - Approved by NINDS July 2014
  - Approved by CMS Sep 2014
  - Enrolled first patient in Feb 2015
  - Capacity
    - to enroll 3-5000 patients
    - to involve 2-400 sites

- Enrollment
  - Sites approved: 65
  - Interventionists approved: 121
  - Proportion of Vascular Surgeons: 32%
  - Patients enrolled: 586