Update On ACST 2:
When Will We Complete Recruitment:
What Has It Told Us Thus Far:
What Are Its Limitations?

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VEITH, Friday 22nd November 2019
2-43-2-48
Grand Ballroom East

I have no financial disclosures

ACST-2 trial
CEA vs CAS

Collaborators are free to use their usual techniques

ACST-2 Randomisation Form: Single side of A4

Where we are now.... Modern CAS therapy (since the symptomatic trials)

Statins and DAPT lower peri-procedural risk and ..

- Newer stent designs
- Flow reversal (MOMA)
- Direct cervical access (TCAR)
- Greater experience
Two stenting hazards – crossing the lesion + navigating in the aortic arch

Recruitment target = 3600

³464 (96% total)

Mean follow-up 2019
CEA: 4.7 person-years
CAS: 4.7 person-years

ACST-1
126 centres in 30 countries
3120 patients

ACST-2 (first 3120)
33 countries, includes Brazil, Canada, China, Japan, Kazakhstan, USA

ACST-2 and modern CAS therapy

<table>
<thead>
<tr>
<th>Stent use</th>
<th>CPD use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wallstent (Closed) (45%)</td>
<td>Filter (99%)</td>
</tr>
<tr>
<td>Exact</td>
<td>Emboshield</td>
</tr>
<tr>
<td>Adapt</td>
<td>Spider</td>
</tr>
<tr>
<td>Precise (Open) (25%)</td>
<td>Assumet</td>
</tr>
<tr>
<td>Proline® RX</td>
<td>AngioGuard</td>
</tr>
<tr>
<td>RX Aculink</td>
<td>formerly</td>
</tr>
<tr>
<td>VIVEXX</td>
<td>Wirion System</td>
</tr>
<tr>
<td>Zilver</td>
<td>Moema</td>
</tr>
<tr>
<td>Cristallo Ideale (Hybrid) (31%)</td>
<td>Flow Reversal</td>
</tr>
<tr>
<td>Simons Cathet Conical RX</td>
<td>Twin One</td>
</tr>
<tr>
<td>Mer</td>
<td>Viatrac</td>
</tr>
<tr>
<td>Resilience (Membrane) (10%)</td>
<td>None</td>
</tr>
<tr>
<td>XGuard</td>
<td>CPD use</td>
</tr>
</tbody>
</table>

CEA in ACST-2

Anaesthetic

<table>
<thead>
<tr>
<th></th>
<th>GA</th>
<th>LA</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patch</td>
<td>52%</td>
<td>29%</td>
<td>81%</td>
</tr>
<tr>
<td>Shunt use</td>
<td>28%</td>
<td>8%</td>
<td>36%</td>
</tr>
</tbody>
</table>

Total (n=1434)
ACST-2 and modern CAS therapy

<table>
<thead>
<tr>
<th>Stent use</th>
<th>CPD use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Closed cell</td>
<td>Filter 69%</td>
</tr>
<tr>
<td>Open cell</td>
<td>Proximal occlusion 16%</td>
</tr>
<tr>
<td>Hybrid</td>
<td>Distal balloon &lt;1%</td>
</tr>
<tr>
<td>Membrane</td>
<td>None 15%</td>
</tr>
<tr>
<td>Total</td>
<td>1451</td>
</tr>
</tbody>
</table>

ACST-2 Medical therapy at Trial Entry

- 81% lipid-lowering drugs
- 85% anti-hypertensive therapy
- 96% anti-thrombotic (anti-platelet/anti-coagulant)

+ good long-term compliance

ACST-2 Procedural hazards (CEA+CAS) much lower than symptomatic trials

- Disabling and fatal Stroke ≤ 30 days: 1.0%
- Lower than in previous trial of CEA: 1.7% (ACST-1)

Acute stroke or procedural complications, interventions are low-risk

When will ACST-2 be complete?

- Recruitment will be complete in early 2020
- 5-year follow up should be complete by mid-2021 and results will be available later that year

What has it told us so far and what are the limitations?

- Medical therapy in ACST-2 is good (>80%)
- Cerebral protection widely used (85%)
- Flow reversal use quite common (16%)
- Closed cell stents still predominate (45%)
- Membrane-mesh covered stents emerging
Asymptomatic CEA vs CAS trials
Evidence for the future!

<table>
<thead>
<tr>
<th>Trial</th>
<th>Participants (Year)</th>
<th>Follow-up</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>CREST</em></td>
<td>1160 pts (2000-08)</td>
<td>10 yr</td>
<td>complete</td>
</tr>
<tr>
<td><em>ACT-1</em></td>
<td>1450 pts (2005-13)</td>
<td>5 yr</td>
<td>complete</td>
</tr>
<tr>
<td>SPACE-2 phase 1</td>
<td>320 pts (2009-13)</td>
<td>5 yr</td>
<td>planned</td>
</tr>
<tr>
<td>ACST-2</td>
<td>3600 pts (2008-19)</td>
<td>10 yr</td>
<td>planned</td>
</tr>
</tbody>
</table>

Total 6500 patients

*CREST, ACT-1: restricted device choice