Trial Design in Vertebral Artery Origin Stenosis

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Disclosure Information
Robert Taylor, M.D.

I have no relevant discloses

I will discuss the following off label use and/or investigational use in my presentation:

Use of coronary stents for the treatment of vertebral artery origin stenosis

Ongoing Clinical Trials

- VAST (Vertebral Artery Stenting Trial) – Netherlands, Phase II
- VIST (Vertebral artery Ischaemia Stenting Trial) – England, Phase III

VAST – Safety and Feasibility Study, Phase II

- Symptomatic (TIA or stroke) ≥50% stenosis by Doppler, CTA, MRA or angio within 6 months
- Primary outcome – Vascular death, non-fatal MI, non-fatal stroke within 30 days
- Secondary outcomes – vascular death, non-fatal MI or non-fatal stroke during 1 year follow-up. Any stroke related to treated vessel. Degree stenosis at 1 year by CTA and Doppler.
- N = 180

VIST – Randomized prospective trial, Phase III

- Symptomatic (TIA or stroke) ≥50% stenosis by CTA, MRA or angio within 3 months
- Primary outcome – Any fatal or nonfatal stroke in f/u (2-8 years)
- Secondary outcomes
  - Any fatal or nonfatal stroke by 3 months
  - VB stroke, VB stroke/TIA, periprocedure stroke/death, any death, any disabling stroke (mRS≥3), restenosis in f/u, NHS and personal social service costs, quality adjusted life years, cost-effectiveness
- N = 540 (100 in feasibility phase)

VAO Stenosis - Clinical Trial Design

- Arm 1 - Best medical therapy
- Arm 2 - Best medical therapy plus stent placement
- Best medical therapy = SAMPPRIS
  - LDL <70, BP < 140/90, <130/80 if diabetic
  - aspirin 325 mg, clopidogrel 75 mg for 1-6 months
- Balloon-expandable coronary stent
  - New generation drug-eluting (6 mo clopidogrel)
  - New generation bare metal (1 mo clopidogrel)

Operator Experience

- SAMPPRIS – documented 20 cases with short term outcomes
- Perioperative stroke risk of <2%
- Experience with a brachial or radial approach

VAO Stenosis - Clinical Trial Design

- Inclusion Criteria
- Exclusion Criteria
- Primary outcome
- Secondary outcome
- Trial size
- Trial duration

Vertebral artery ostial stent placement for atherosclerotic stenosis in 72 consecutive patients: clinical outcomes and follow-up results

- Group 1 - 25 Transient Neurological Deficit
- Group 2 - 24 Posterior Circulation Stroke
- Group 3 - 13 “High Risk” Asymptomatic
- Group 4 - 10 Hemodynamic Stroke From Chronic Carotid Occlusion
- Treated over ~ 6 years, 10 per year

Taylor et al. Neuroradiology. 2009 Aug;51(8):531-9

Inclusion Criteria

- Stroke or TIA referable to the lesion within 30 days (SAMMPRIS), 3 months (VIST)
- 70-99% symptomatic stenosis by angiography
- Possibly even high risk e.g. other vert is occluded, ends in PICA, or also has severe stenosis, no or small PComms
- TIA needs clear definition e.g. exclude isolated vertigo

Exclusions

- Tandem intracranial and ECVAO stenosis
- Tandem V1 lesions okay
- Asymptomatic lesions
- Dissections

Is This More than 1 Trial?

- Enrolling event - stroke
- Primary outcome – stroke/vascular death

- Enrolling event – Recurrent TIA
- Primary outcome – Reduction in TIA frequency, quality of life measures

Secondary outcomes

- VB stroke
- VB stroke/TIA
- TIA frequency
- periprocedure stroke/death
- any death
- any disabling stroke
- restenosis in f/u
- personal social service costs
- quality adjusted life years
- cost-effectiveness

Trial Size

- VIST, N = 540, 2- 8 year f/u
- SAMMPRIS, N= 764 planned
  - Decrease stroke by 35% over 2 years
- ACAS, N = 1659, median 2.7 yr f/u

- To understand trial size, we need natural history data on medical therapy!

Trial Duration

- 50 centers
- 1000 patients
- 2-10 eligible patients per year per center
- Duration – 2 years to 10 years to enroll