An Overview of SPARCL – Stroke Prevention by Aggressive Reduction in Cholesterol Levels

SPARCL Trial Overview
A multi-center prospective, randomized, doubled blinded, placebo-controlled trial evaluating the efficacy of high dose atorvastatin for the prevention of stroke recurrence (fatal and non fatal) after a recent stroke or transient ischemic attack (TIA) in patients with “normal” cholesterol levels (LDL: 2.6-4.9 mmol/L) and NO known history of coronary heart disease. (intention to treat analysis; all patients enrolled were included in final analysis)

- two treatment arms: • atorvastatin 80mg daily (n=2365) • placebo (n=2366)
- 4,731 patients were followed for 4.9 years (4.0-6.6yrs) with the following characteristics:
  - males 46%, & females with previous stroke/TIA 30% (ischemic 46%, hemorrhagic 25%, embolic, lacunar & cryptogenic within 6-12 months of enrollment),
  - average time since entry event: 87.1 days (atorvastatin), 84.3 days (placebo)*significant difference
  - age: mean ~63 years
  - Baseline LDL mean: 3.4 mmol/l (Range: 2.6-4.9mmol/l) BMI: 27.5 kg/m2 BP: 139/82 mm Hg
  - smokers 19%, former smokers 40%, hypertension 62%, history of diabetes –17%, Framingham not calculated, estimated 10%

Of Note:
- Table 1: SPARCL Results

| Endpoints | Atorvastatin% (n=2365) | Placebo% (n=2366) | ARR % | RRR % | NNT/49 yrs | p value
|------------|------------------------|-----------------|-------|--------|------------|--------|
| Nonfatal or fatal stroke
  *only first event for each patient counted |
| 11.2 (265 events) | 13.1 (311 events) | 1.9 | 15 | 53 | 0.05 |
| TIA | 6.5 | 8.8 | 2.3 | 26 | 43 | 0.004 |
| **Major Coronary Event** | 3.4 | 5.1 | 1.7 | 33 | 59 | 0.006 |
| **Major Cardiovascular Event** & Stroke | 14.1 | 17.2 | 3.1 | 18 | 32 | 0.005 |
| Death (any cause) | 9.1 | 8.9 | 0.2 | 2 | NS | 0.77 |

* unadjusted p values calculated by the log-rank test, adjusted treatment hazards ratios, 95% CI, and p values available in original study
** includes death from cardiac causes, nonfatal MI or resuscitation after cardiac arrest

Table 1: SPARCL Results

We what we know and what these results add to that knowledge:
- A meta analysis of previous RCTs on the effects of statins on primary stroke prevention suggest that statins reduce the overall incidence of stroke in hyperlipidemic patients both with and without CHD (RR:0.75 & 0.77 respectively).2
- HPS showed statin therapy (simvastatin 40mg vs placebo) reduced the rate of primary and/or secondary (fatal or non-fatal) stroke in patients with CHD (4.3% simvastatin 40mg vs placebo, NNT=72) regardless of baseline lipid levels(but not those with pre-existing stroke)3
- SPARCL aggressive lipid therapy (atorvastatin 80mg/d) appears to reduce the overall incidence of secondary ischemic/unclassified strokes and “major cardiovascular events” in patients without known CHD
- Magnitude of benefit: one less secondary stroke for every 53 patients (with a recent stroke/TIA) treated for 4.9 years.
- Magnitude of harm: one more hemorrhagic stroke for every 112 patients treated atorvastatin 80mg for 4.9 years.

Heads-Up:
1) Excluded 29.1% (1939) of the initially screened population, including the exclusion of patients with atrial fibrillation and other cardiac sources of embolism therefore may not be able to extrapolate benefit of routine high-dose atorvastatin to ischemic strokes of cardioembolic origin which is generally the cause of 1 in 5 ischemic strokes4
2) Significant reduction in incidence of fatal stroke for 0.5%. Only, with a non-significant reduction in non-fatal strokes3,5
3) Unknown whether lower dosages of atorvastatin would have less harm & a similar benefit (atorvastatin 10mg=$800; 80mg=$1050 per yr)
4) Overall benefit modest in heterogeneous population
5) Since the number of nonfatal stroke was not different between groups, it would be interesting to see if a difference in stroke severity was present (preliminary data presented by Goldstein at the ANA 131st Meeting suggests ↓ stroke severity)

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References: