Key points regarding:

CAD-REAL

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Disclosures

• Research Grants - National Institutes of Health
  – NHLBI
  – NIDDK
  – BD2K consortium

• Speaker’s Bureau
  – Boehringer-Ingelheim

• Consultant
  – Amgen, Boehringer-Ingelheim
Background

- Pharmacokinetic studies have noted higher plasma levels of statins in patients of Asian descent as compared to other ethnic groups, even when comparable doses of statins are used.

- For this reason, some statin labels and some regulatory bodies suggest using lower doses of statins in Asian patients.
Background

- Patients of Asian descent are often not treated with high dose statin therapy, even in clinically appropriate situations.

- Demonstrating safety and efficacy of high dose statin therapy in Asian populations is therefore, of utmost importance.
The CAD REAL study adds important clinical trial evidence in support of high dose statin therapy in Asian populations.
What we learned from this trial

• In an Asian CAD population, pitavastatin 4 mg daily reduced the composite primary outcome (cardiovascular death, myocardial infarction, ischemic stroke, and unstable angina) more than pitavastatin 1 mg daily
  – At 3 years, ARR = 1.1%; RRR = 19%; NNT = 63

• Pitavastatin 4 mg daily also reduced total mortality
  – At 3 years, ARR = 0.9%; RRR = 27%; NNT = 111

• Both doses reduced LDL-c
  – Pitavastatin 4 mg daily final LDL-c was 76.6 mg/dL
  – Pitavastatin 1 mg final LDL-c was 91 mg/dL
What else we learned from this trial

• Pitavastatin 4 mg daily also increased HDL-c, reduced triglycerides and reduced hs-CRP more than pitavastatin 1 mg

• Importantly, pitavastatin 4 mg daily was well tolerated
  – Muscle complaints were the only difference between groups (0.7% vs. 1.9%)
  – No difference in rhabdomyolysis or any other AE
# Intensity of Statin Therapy

<table>
<thead>
<tr>
<th>High-Intensity Statin Therapy</th>
<th>Moderate-Intensity Statin Therapy</th>
<th>Low-Intensity Statin Therapy</th>
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<tbody>
<tr>
<td>Daily dose lowers LDL-C on average, by approximately ≥50%</td>
<td>Daily dose lowers LDL-C on average, by approximately 30% to &lt;50%</td>
<td>Daily dose lowers LDL-C on average, by &lt;30%</td>
</tr>
<tr>
<td><strong>Atorvastatin</strong> (40†)-80 mg</td>
<td><strong>Atorvastatin 10 (20) mg</strong></td>
<td><strong>Simvastatin 10 mg</strong></td>
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<tr>
<td><strong>Rosuvastatin</strong> 20 (40) mg</td>
<td><strong>Rosuvastatin (5) 10 mg</strong></td>
<td><strong>Pravastatin 10-20 mg</strong></td>
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<td><strong>Simvastatin 20-40 mg‡</strong></td>
<td><strong>Lovastatin 20 mg</strong></td>
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<td><strong>Pravastatin 40 (80) mg</strong></td>
<td><strong>Fluvastatin 20-40 mg</strong></td>
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<td><strong>Lovastatin 40 mg</strong></td>
<td><strong>Pitavastatin 1 mg</strong></td>
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<td><strong>Fluvastatin XL 80 mg</strong></td>
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<td><strong>Fluvastatin 40 mg bid</strong></td>
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<td><strong>Pitavastatin 2-4 mg</strong></td>
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What we still don’t know...

• Would outcomes have been improved with even greater LDL-c reduction?
• How much better would outcomes have been if high intensity statin therapy (> 50% LDL-c reduction) had been used, as recommended by the 2013 AHA-ACC cholesterol guidelines?
• Would high intensity statin therapy have been as well tolerated?
• Do these data translate to other statins
Take home points

- High dose pitavastatin therapy (4 mg daily) improves cardiovascular outcomes more than low dose pitavastatin (1 mg daily), and is also associated with a total mortality reduction.

- High dose pitavastatin therapy is well tolerated.
  - Tolerability of higher statin doses in Asian populations had been questioned.

- There has been substantial reluctance to use higher dose statins in Asian patients. This trial should give comfort that this strategy is safe, well tolerated, and beneficial.

- This trial further supports intensive LDL-c lowering with high dose statins, including in Asian populations.