Pharmacy Pearls

February 2020

Lipid Management- Vascepa® and Statin Intolerance

Contact: AHPPharmacist@urmc.rochester.edu

Vascepa® for Hypertriglyceridemia

Originally approved in 2011 for severe hypertriglyceridemia, the results of the REDUCE-IT trial have prompted a renewed interest in the omega-3 product, icosapent ethyl (Vascepa®). Relative to placebo, Vascepa® demonstrated a 25% decrease in CV events when used as adjunct to statin therapy in patients with moderately elevated triglycerides (TG). Though promising, these results are somewhat puzzling as this is the first and only omega-3 agent to show a clear CV benefit.

REDUCE-IT Trial Summary

Inclusion Criteria

- ≥45 years with established CVD (secondary prevention) *or* ≥50 years with DM and at least one additional CV risk factor (primary prevention)
- On statin therapy with fasting TG 150 – 499 mg/dl *and* LDL 41 – 100 mg/dl

Results

- The study followed 8179 patients for a median for 4.9 years. The majority of patients were white (90%) males (70%) with a median age of 64 years. A total of 94% of the population were taking moderate or high intensity statins and 70% were being treated for secondary prevention. **The median baseline LDL was 75 mg/dl.**

Endpoint	HR (95%CI)	NNT x 4.9 years
Composite of CV death, MI, stroke, revascularization, or unstable MI	0.75 (0.68 – 0.83)	21
CV death	0.8 (0.66 – 0.98)	111
Non-fatal MI	0.7 (0.59 – 0.82)	44
Non-fatal stroke	0.71 (0.54 – 0.94)	125
Revascularization	0.66 (0.58 – 0.76)	25
Unstable angina	0.68 (0.53 – 0.87)	83

- After 1 year, TG decreased 18% in the treatment group and increased 2% in the placebo group. LDL increased 3% in the treatment group and 10% in the placebo group.
- Vascepa® was well tolerated. The most common non-serious adverse effects which occurred more frequently than placebo were peripheral edema (6.5% vs. 5.0% placebo) and constipation (5.4% vs. 3.6%).
- A small but significantly higher incidence of a-fib (5.3% vs. 3.9% placebo) and hospitalization for a-fib or flutter (3.1% vs. 2.1% placebo) was observed with Vascepa®. Likewise, a small increased risk of serious bleeding was observed in the treatment group (2.7% vs. 2.1% placebo).

View AHP's full Lipid Management Guideline here

Role in Therapy

- May be considered for patients with **TG >150 *AND* LDL <100 despite moderate-high intensity statin**
- Results cannot be extrapolated to patients with moderately elevated TG *AND* elevated LDL or those who decline statin therapy.
- Subgroup analysis suggests Vascepa® may be most beneficial for secondary prevention.
- **Prior studies have failed to show a CV benefit of other omega-3 products.** It has been suggested that the CV benefits observed with Vascepa® are due to the fact that it contains EPA only rather than the traditional EPA/DHA combination. **It has been hypothesized that DHA raises LDL and thus EPA alone may reduce CV risk**, however the true mechanism of benefit remains unclear. While the results of REDUCE-IT are promising, findings from ongoing studies will further direct the level of confidence in these results.

Cost: $350 - $400 per month

Statin Intolerance

Statin-Associated Muscle Symptoms (SAMS):

Incidence: While SAMS are one of the most common patient-reported adverse effects associated with statin use, this is still considered a relatively rare side effect (reported incidence from available data: myalgias = 3-5%, myopathy = 0.1-0.2%, and rhabdomyolysis = 0.01%). Additionally, these symptoms can often be attributed to other causes (i.e. hypothyroidism, recent exercise, clinically significant drug interactions that increase statin exposure, etc.) and patients can usually tolerate an alternative statin or dose reduction.

Diagnosis: It is important to avoid labeling patients as "statin intolerant" unless they truly are, given statins' overwhelming CV benefit. Patients should be considered statin intolerant when:

- Muscle-related symptoms have resolved with statin discontinuation
  AND
- Symptoms recurred with re-challenge of 2-3 other statins that
  - Use different metabolic pathways (i.e., have different lipophilicity)
    AND
  - 1 of which was prescribed at the lowest approved dose

Patient Education: Educating patients regarding muscle symptoms that can be attributed to statins is vital for appropriate diagnosis and management. Common presentation of SAMS includes:

- Symptoms occurring in the proximal, large muscles such as the thighs, buttocks, calves, and back
- Typically symmetrical as opposed to unilateral

Strategies to Address SAMS:

2-6 week statin washout period

Switch to another statin

Pravastatin or **rosuvastatin**

- Hydrophilic statins (theoretically penetrate muscle less than lipophilic statins)
- Typically have less drug interactions

Reduce dose of current statin

Consider an **alternative dosing strategy**
(for statins with long half-lives)

Atorvastatin or **rosuvastatin**

Dosing strategies include:
- Every other day
- 3 times per week
- Once weekly

Although these are off-label doses, some statin is better than no statin
- Intermittent statin dosing + ezetimibe can reduce LDL >30%

Avoid CoQ10 *(routine use not recommended)*:
- Lack of demonstrated clinical data to support its use (benefit is theoretical)
- Can be expensive and contributes to polypharmacy
- Safety and efficacy is not regulated by the FDA